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See related articles, “HLA-DRB1*15:01 and HLA-DRB3*02:02 in PLA2R-Related Membranous Nephropathy,” and “MHC Class II Risk Alleles and Amino Acid Residues in Idiopathic Membranous Nephropathy,” on pages 1642–1650, and 1651–1664, respectively.

Lesson Learned in Mortality and Kidney Transplant Outcomes among Pediatric Dialysis Patients

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I have a dream that my four little children will one day live in a nation where they will not be judged by the color of their skin, but by the content of their character (Martin Luther King Jr.).

The terms race and ethnicity carry complex nuances that reflect culture, history, socioeconomic, and political status. These nuances are juxtaposed with epigenetic changes due to differing psychologic and physical environmental influences and differing frequencies of select genetic variants that reflect important linkages to ancestral geographic origins.¹ These complexities contribute to population differences in clinical

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outcomes, including survival. Studies of adult patients on dialysis show a survival advantage in racial/ethnic minority patients, despite a higher prevalence of worse pre-ESRD and ESRD quality care metrics and higher rates of traditional cardiovascular risk factors for premature mortality.^{2,3} This survival advantage has been most pronounced in patients of Hispanic ethnicity.^{4,5} Recent data have shown that this survival advantage varies by age as well.^{5–8} Kucirka *et al.*⁶ compared two racial groups, black and white patients on dialysis, within the US Renal Data System (USRDS) and showed that blacks displayed a survival advantage that was limited to patients older than 50 years old. For patients <50 years of age, blacks had an increased risk of mortality compared with their white peers. By parsing out race and ethnicity and then comparing Hispanic patients with non-Hispanic whites, Arce *et al.*⁵ showed a survival advantage in Hispanic patients that was progressively greater with decreasing age. This advantage was largely attenuated, although still present, after accounting for decreased transplantation rates among Hispanic patients.

Yan *et al.*⁷ reported that, after adjusting for transplantation, there was a survival advantage across all age groups for Hispanic patients but for blacks, an increased mortality rate in the 18- to 30-year-old age group. Rhee *et al.*⁸ reported similar findings in a cohort of over 130,000 patients with extensive laboratory data in a large national dialysis organization. Compared with non-Hispanic white patients on dialysis, there was a survival advantage for Hispanic patients across all age groups, whereas the survival advantage in blacks was limited to those older than 60 years of age. Although the survival advantage in adult Hispanic patients on dialysis is robust across all age categories, younger blacks experience a decreased or similar survival to non-Hispanic white patients. Thus, age is a major modifier of the relationship between race, ethnicity, and survival, but most studies have been limited to adults and have not looked closely at the pediatric population.

In this issue of the *Journal of the American Society of Nephrology*, Ku *et al.*⁹ explore in detail mortality in different racial/ethnic groups in the pediatric dialysis population. In a USRDS analysis of 12,123 pediatric patients on dialysis, they found a survival advantage in Hispanic children but decreased survival in non-Hispanic black children compared with non-Hispanic white children.⁹ However, after further adjusting for transplantation as a time-dependent covariate, they found that the survival advantage in Hispanic children did not significantly change, whereas the decreased survival among non-Hispanic black children was attenuated to a survival rate similar to that of non-Hispanic white children.⁹ Accounting for differences in transplantation rates is important, because there may be different rates by race/ethnicity of either very ill or very healthy children who are transplanted and therefore, removed from the dialysis cohort. Furthermore, similar to adult studies, black and Hispanic pediatric patients experience lower rates of transplantation and waitlist activation.^{10,11} The results of the work by Ku *et al.*⁹ suggest that the decreased survival seen in black children is mainly accounted for by differential transplantation rates. This finding

is of importance, because it suggests that, by addressing the disparities in transplantation, we may also improve the disparities in survival for pediatric patients treated with dialysis.

This study has several limitations. First, there are significant racial differences in the etiology of ESRD in their cohort, which may contribute to some of the observed racial differences in survival of children, despite attempts to statistically adjust for cause of ESRD. Second, there may be a variety of unique resilience factors that may influence survival in Hispanic children, such as selective healthy migrants for those who recently came to the United States and/or social network, familial, and cultural factors.¹² Third, there may be residual confounding related to unmeasured factors.

However, these limitations are balanced by several strengths. This is the largest cohort to explore survival by race/ethnicity in children, and it is bolstered by the large number of clinical outcomes that provide the power to adjust for multiple potential confounders. By using non-Hispanic white children as the reference group rather than white children (non-Hispanic and Hispanic), they eliminated a possible bias of mixing two groups of children who have a differing survival rate. Also, given that the children in their cohort are likely to have been born in the United States, the healthy migrant and salmon biases (sicker individuals returning home)¹³ are less likely to explain the observed Hispanic survival advantage in children. Finally, they adjusted their analyses for median neighborhood income, an important variable that has been reported to influence dialysis outcomes in adults.¹⁴

Similar to findings by Ku *et al.*,⁹ a recent study by Laster *et al.*¹⁵ explored how mortality might differ by race/ethnicity using a smaller population of 2697 pediatric patients from a large dialysis organization. They found that black children experienced increased mortality compared with non-Hispanic white children, whereas Hispanic children had similar or lower mortality risk compared with non-Hispanic white children.¹⁵ Contrary to the findings by Ku *et al.*⁹ in competing risk analysis, transplantation did not seem to mediate the racial/ethnic differences in survival. In considering adult findings that inflammatory and nutritional factors contribute to differences in survival, Laster *et al.*¹⁵ also assessed whether such factors modified the mortality relationship and found that the differences in mortality persisted even after stratification for these factors.

Thus, it is unclear whether adjusted differences in survival for children treated with dialysis reflect differences in underlying disease etiology, higher rates of being uninsured or underinsured, a more limited ability to provide comprehensive family support, or other. Potential factors posited to affect differences in adults, such as survival bias (variations in the health of those who make it to dialysis), psychosocial resilience, and/or permissive or effect-modifying biologic resilience,¹⁶ may also exist in pediatric patients, but if so, they are not likely to be expressed to the same extent as in adults.

In summary, the findings from the work by Ku *et al.*⁹ represent a detailed analysis of racial/ethnic survival

differences in the largest cohort of pediatric patients on dialysis to date. This study adjusted for not only traditional demographic and clinical factors but also, community-level income as a proxy for area-level social determinants of health. They then further adjusted for renal transplantation and found that the robust report of enhanced survival for Hispanics across all ages of adults extended to the pediatric population, whereas the initial noted increased mortality in black patients was largely attenuated by adjustments for transplantation. This study provides insight into factors affecting mortality across race and ethnicity for children on dialysis and further impetus to strive toward equitable transplantation rates in the pediatric population.

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DISCLOSURES

None.

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See related article, "Racial and Ethnic Disparities in Survival of Children with ESRD," on pages 1584–1591.