The presence of traits for hemoglobinopathy such as that for sickle cell disease may help explain the need for greater doses of anemia medications administered to African Americans undergoing dialysis compared with Caucasians.

To reach the same level of hemoglobin, African American dialysis patients with hemoglobinopathy traits required higher doses of erythropoiesis-stimulating agents (ESAs) during dialysis than other African American patients, according to a *Journal of the American Society of Nephrology* study.

“This research is important because it is the largest study to evaluate how sickle cell trait affects anemia treatment in African American hemodialysis patients,” said first author Vimal Delerebail, MD, MPH, of the University of North Carolina at Chapel Hill and the UNC Kidney Center.

*Sickle cell study results*

Sickle cell trait represents the carrier state of sickle cell disease and is present in an estimated 6 percent to 8 percent of African Americans. While sickle cell disease is characterized by abnormally shaped red blood cells that can block blood flow and cause organ damage, the carrier state—called sickle cell trait—is generally thought to be benign. Kidney abnormalities have been reported in some individuals with sickle cell trait, however.

Derebail and his team wondered whether the presence of sickle cell trait among African Americans might impact ESA dosing in those on dialysis, many of whom require higher doses than their Caucasian counterparts. Previous research had shown that uremic toxins alter erythrocytes. Transit through a hemodialysis circuit could predispose to sickling of red blood cells containing sickle cell trait as a result of exposure to lower temperature, lower partial pressure of oxygen, and physical stressors of the hemodialysis filter. Transient sickling events in erythrocytes may lead to a reduced life span of the cells.

In a cross-sectional, observational study, Derebail and his colleagues examined laboratory and clinical data over 6 months for 52 African American and 20 Caucasian hemodialysis patients. African Americans required 16% higher ESA doses than their Caucasian counterparts.

Pediatric CKD Progression Model Identifies Children at Highest Risk for ESRD

By Kurtis Pivert

A new model could predict which children with chronic kidney disease (CKD) are at highest risk for progressing to end stage renal disease (ESRD) well before they lose renal function. Using existing patient data, the composite scoring system would facilitate early intervention, giving nephrologists the opportunity to slow the disease course. The model, recently published in the *Clinical Journal of the American Society of Nephrology*, is the first specifically designed to assess the unique characteristics of children with CKD (1). Although further validation in a larger population is needed, the system could be a valuable resource for the pediatric kidney care team.

“Clinicians could easily apply this tool in their practice, since our model uses routinely available clinical and laboratory data, and can predict the long-term risk for renal impairment with accuracy,” said senior author Ed-
Sickle Cell Trait

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months in 2011 for 5319 adult African American hemodialysis patients, 542 (10.2 percent) of whom had sickle cell trait and 129 (2.4 percent) of whom had hemoglobin C trait. A total of 5002 patients (10.3 percent sickle cell trait and 2.4 percent hemoglobin C trait) received ESAs. (In people with hemoglobin C trait, some of the hemoglobin in the blood is an abnormal form, called hemoglobin C. People with hemoglobin C disease have mostly hemoglobin C, which can reduce the number and size of red blood cells in the body, causing mild anemia.)

The researchers found that patients with hemoglobinopathy traits received higher median doses of ESA than patients with normal hemoglobin (4737.4 vs. 4364.1 units/treatment). Hemoglobinopathy traits were linked with 13.2 percent increased ESA use in African Americans undergoing dialysis, the findings may have important policy implications. 

Undergoing dialysis, the findings may have increased ESA use in African Americans with hemoglobinopathy traits, the cost of which was $16.8 and $33.5 million per year.

The study also found that sickle cell trait was slightly more common among dialysis patients, present in 10 percent of study participants compared with 6.5 percent to 8.7 percent in the general African American population.

Bundled payment adjustments for sickle cell disease, but not trait

By connecting sickle cell trait with increased ESA use in African Americans undergoing dialysis, the findings may have important policy implications.

Presently, Medicare bundled payments for dialysis allow adjustment for several chronic diseases including sickle cell disease, but not sickle cell trait, which is far more common than sickle cell disease and other potential modifiers of anemia,” Derebail said. “While we don’t know whether there are any adverse consequences to this higher dose of medication yet, further policies and decisions regarding management of anemia in dialysis patients should take into account these findings.”

The researchers calculated that with the average wholesale price of ESA at $1.518 per 100 units, and the average ESA dose being 6100 units per treatment in patients with normal hemoglobin, these traits would account for a $12.10 increase in cost of each dialysis treatment. Conservatively estimating an average of 140 treatments yearly, this increase amounts to an incremental expense of more than $1 million annually in the study cohort. When the findings are extrapolated to the U.S. hemodialysis population of more than 140,000 African Americans who fall within the group of 7 percent to 14 percent with hemoglobinopathy traits, the cost of ESAs attributable to these traits is between $16.8 and $33.5 million per year.

“In addition to considering the cost implications of this increased ESA requirement, more studies are required to ascertain the mechanism for increased ESA requirement in sickle cell trait as well as hemoglobin C trait,” Ataga said.

Because the study also revealed that sickle cell trait is somewhat more common in the dialysis population than in the general population, it raises the question of whether sickle trait might contribute to kidney disease. Additional studies are needed to test this possibility, the researchers said.

Study co-authors include Eduardo Lacson, Jr., MD, Abhijit Kshirsagar, MD, Nigel Key, MB ChB, Susan Hogan, PhD, Raymond Hakim, MD, Ann Mooney, MSN, Chinu Jani, SC, Curtis Johnson, Yichun Hu, MS, Ronald Falk, MD, and J. Michael Lazarus, MD.

Disclosures: Drs. Lacson, Hakim, and Lazarus and Ms. Mooney were employed by FMCNA, the sponsor, at the time of the study. Mr. Johnson and Mr. Jani are employed by Spectra Laboratories, Inc.