The field of neonatal acute kidney injury (AKI) is in its infancy, but some reports indicate that up to one-quarter of newborns in intensive care units may develop AKI, which puts them at increased risk of poor clinical outcomes and even premature death. Premature newborns have an elevated risk of developing chronic kidney disease and end stage renal failure compared with term infants, and AKI may possibly contribute to this risk.

Although detecting AKI in newborns is critical for their current and future health, it can be challenging to achieve with current serum creatinine–based tests, in part because serum creatinine levels on postnatal day 1 reflect maternal levels, which decline over time depending on gestational age. Now, new research published in the Clinical Journal of the American Society of Nephrology indicates that several proteins are excreted differently in preterm infants with kidney injury compared with those with healthy kidneys. The biomarkers may be used to develop better diagnostics related to kidney health in newborns.

“Having better diagnostic tests to diagnose kidney injury can have an important impact on how we care for infants, how we prognosticate outcomes, and how we design studies to prevent and/or mitigate AKI,” said David Askenazi MD, an associate professor in the University of Alabama at Birmingham’s Department of Pediatrics and director of the university’s Pediatric and Infant Center for Acute Nephrology.

Using single drops of urine from 113 preterm infants (birth weight ≤1200 g and/or ≤31 weeks gestational age), Askenazi and his colleagues prospectively examined the potential of 14 urine proteins for indicating the presence of kidney damage. Among the 113 infants included in the study, 28 (25%) were diagnosed with AKI. Death occurred in 13 (11.5%) infants. Babies with AKI had smaller birth length, were less likely to be born from mothers with preeclampsia [1/28 (4%) vs. 32/85 (38%)], and were more likely to have an umbilical artery catheter [18/28 (64%) vs. 29/85 (34%)].

The researchers found that several of the urine proteins measured during the mid-1970s have suggested steady increases in the percentage of Americans with advanced chronic kidney disease (CKD). But that may be changing, as an updated data analysis finds no significant increase in CKD in the US adult population since the early 2000s, according to an updated analysis of population-based data. “In a reversal of prior trends, there has been no appreciable increase in the prevalence of stage 3 and 4 CKD in the US population during the most recent decade,” concludes the new report, published by the Annals of Internal Medicine last month.

It’s a welcome finding that is consistent with recent evidence of stabilization in incidence of end stage renal disease (ESRD). While CKD prevalence has remained stable in most subgroups, the investigators strike a note of concern regarding continued increase in prevalence of CKD among African Americans.

Study updates nationwide data on CKD trends

The study by the Centers for Disease Control and Prevention, published in the Annals of Internal Medicine last month, indicates that the percentage of Americans with CKD has stabilized since the early 2000s, according to an updated analysis of population-based data. “In a reversal of prior trends, there has been no appreciable increase in the prevalence of stage 3 and 4 CKD in the US population during the most recent decade,” concludes the new report, published by the Annals of Internal Medicine last month.

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CKD Prevalence

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crol and Prevention’s Chronic Kidney Disease Surveillance Team analyzed trends in CKD prevalence among US adults. The CKD Surveillance System provides a centralized source of data for use in tracking the full scope of kidney disease, including risk factors, impact on population health, and the healthcare system’s capacity for managing CKD. In addition to the CDC, the CKD Surveillance System is supported by research teams at the University of California, San Francisco, led by Neil Powe, MD, MPH, MBA; and the University of California, San Francisco, led by Rajiv Saran, MD.

The CKD Surveillance Team analyzed National Health and Nutrition Examination Survey (NHANES) data from 1988 to 1994, and every two years from 1999 to 2012. Stage 3 or 4 CKD was defined as an estimated glomerular filtration rate (eGFR) of 30 mg/min/1.73 m². The eGFR estimates were derived from the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, using calibrated serum creatinine measurements.

The study was supported by the Centers for Disease Control and Prevention and the National Institutes of Health. In addition, lead author Daniel Murphy, MD, previously at UCSF and now a resident at the University of Minnesota—received support from the American Society of Nephrology Foundation for Kidney Research Student Scholar Grant Program.

The results support a steady increase in the prevalence of CKD among all races and ages. From NHANES data from the late 1980s through the early 2000s, the crude prevalence of stage 3 or 4 CKD rose from 4.8% in 1988–94, to 5.3% in 1999–2000, to 6.4% in 2001–02, to 6.9% in 2003–04.

Since then, there has been no further change in CKD prevalence. From NHANES 2005–06 to 2011–12, the figures have remained in the range of 6.4% to 6.9%.

In 2000, the prevalence levelled off across age groups, estimates were substantially higher in older Americans. In 2011–12, the figures were 3.8% in participants aged 40 to 64 years, 21.7% in those aged 65 to 79, and 51.1% in those aged 80 years and older. The pattern was similar for participants with and without diabetes—peak prevalences were about 19% and 5%, respectively.

In non-Hispanic white participants, the figures followed the overall population trend: peaking at about 8% in 2005–06 and remaining stable thereafter. However, there was evidence of a continued increase in prevalence among non-Hispanic blacks: from 3.7% in 1988–94, to 4.9% in 2003–04, to 6.2% in 2011–12. All of these patterns—including the persistent rise in CKD among non-Hispanic blacks—persisted in adjusted analyses.

A secondary outcome evaluated the complete spectrum of CKD stages (1 to 5), including individuals with eGFR of 60 mL/ min/1.73 m² or higher who had a marker of kidney damage (urine-to-creatinine ratio of 30 mg/g or higher). The results showed a similar pattern: starting in the early 2000s, overall crude prevalence remained stable at about 14%, while the adjusted prevalence decreased slightly.

As in the main analysis, the prevalence of CKD (all stages) continues to increase among the non-Hispanic black population, although there was no statistically significant interaction. Similar patterns also prevailed in a sensitivity analysis using the Modification of Diet in Renal Disease (MDRD) Study equation to calculate eGFR.

Stabilization is consistent with trends in ESRD

Because nearly all cases of ESRD are preceded by CKD, reducing the prevalence of CKD would seem to be a critical step toward reducing the number of cases of ESRD. After decades of increases, the incidence of ESRD has decreased since the early 2000s. According to the 2012 US Renal Data System report, the adjusted incidence rate of ESRD decreased from 386 cases per million persons per year in 2003 to 351 per million in 2013. “There is no room for complacency, however,” added Saran, who is Director of the U.S. Renal Disease Coordination Center. “Falling mortality rates in the general population could affect future prevalence of CKD in an aging population or in specific subgroups, and should continue to be monitored closely along with intensive efforts at prevention, earlier detection, and management.”

Previous reports have suggested continued increases in the prevalence of CKD—up to 5% per year. However, these studies have not incorporated data from more recent years.

Of course the analysis of NHANES data can’t explain why CKD prevalence has flattened out—but recent improvements in medical management seem likely to play a role, according to an accompanying editorial by Linda E. Fried, MD, MPH, and Paul M. Palefsky, MD, of the University of Pittsburgh. “One can speculate that it is related to improvements in blood pressure and glycemic control among high-risk populations and increased use of interventions blocking the renin-angiotensin system in patients with proteinuria,” Drs. Fried and Palefsky write. “If so, this would support intensified efforts to increase awareness and treatment of persons with CKD.”

When trying to decrease ESRD, the first thing you want to do is decrease the prevalence of earlier stages of the disease in addition to slowing progression of disease,” Powe commented. “This reversal of the trend of rising CKD rates should ultimately mean less end stage renal failure and its morbidity consequences and excess mortality. The kidney disease community should be commended for this scientific progress.” The researchers note evidence of similar trends in CKD from other countries, notably including England.

“For nephrologists, it’s exciting to have these data supporting the effectiveness of our interventions to prevent and slow the progression of CKD,” commented Chi-yun Hsu, MD, of UCSF—along with Powe, one of the study’s senior authors. “Our efforts are paying off in terms of combating kidney disease in the population.”

Meanwhile, the apparent continued increase in CKD prevalence among African Americans is a major concern. “This is the group with the highest risk of developing end stage kidney disease, and needing to have kidney replacement therapy,” Powe said. “We must continue to reduce the times the risk of developing end stage kidney failure than any other racial or ethnic group. Genetics, quality of care and environmental factors together probably play a role.”

The new finding offers a backdrop for racial differences in the progression from CKD to ESRD, as well as recent data on the genetic factors (i.e., APO1 gene variants) contributing to racial differences in CKD risk. Ongoing research is needed—particularly in light of recent evidence that while ESRD incidence remains higher in the black population, it has decreased much faster than in whites. The CKD Surveillance Team calls for “careful monitoring” of CKD in the African American population, as well as studies to understand the pathophysiology of advanced CKD in blacks.

“If these findings highlight the importance of getting all eligible patients into proper treatment for their conditions,” Hsu said. “As nephrologists, we have a real opportunity to promote better CKD awareness and care among internists and primary care physicians who really provide the major care antecedent to development of CKD, as well as much of the care given to diagnosed CKD patients.”