Vitamin D deficiency is nearly universal in patients who have hypoalbuminemia (≤ 3.1 g/dL) and who start dialysis during the winter, a new study has found (Bhan I, et al. Clinical measures identify vitamin D deficiency in dialysis. Clin J Am Soc Nephrol 2010; 5:460-467).

“We were hoping to see if clinical data that are readily available to clinicians taking care of patients starting dialysis could identify individuals likely to have vitamin D deficiency,” said first author Ishir Bhan, MD, of the Massachusetts General Hospital in Boston. “While we cannot predict this with 100 percent accuracy, we did identify a subpopulation at extremely high risk of deficiency.”

Bhan’s study looked at parameters that can reveal which kidney disease patients starting hemodialysis will almost certainly be vitamin D deficient (defined by serum levels of 25-hydroxyvitamin D).

Vitamin D levels in kidney disease patients

Impaired metabolism of vitamin D is among the most recognized disorders associated with chronic kidney disease (CKD), and 50–90 percent of patients with end stage renal disease (ESRD) are vitamin D deficient. Although low levels of 25-hydroxyvitamin D in the blood are associated with increased mortality in patients with ESRD, testing for the vitamin is expensive and not routinely performed in these individuals. If commonly collected clinical characteristics could be used to predict the risk of vitamin D deficiency in ESRD

ESRD Bundling Rule Garners Many Comments

By Caroline Jennette and Bradley Layton

Almost everyone in the renal community has heard the steady grumbling about the new Prospective Payment System (PPS) or “bundle” set to change the landscape for dialysis reimbursement in 2011. Reactions to the proposal have run the gamut from enthusiastic to outraged. A number of stakeholders, including patient advocates, health care providers, and professional organizations, added their voice to the federal comment submission process that ended late last year.

Before a final rule is created, Congress is legally mandated to have an open submission period to garner ideas, suggestions, and concerns from the public on proposed regulations. Submitted comments are used by the rulemaking body to justify how decisions are made for the final rule.

In many cases, the public doesn’t scan the Federal Register and provide comments—this process is usually left to interest groups and paid lobbyists. But the creation of a new payment system for dialysis—a financially and emotionally charged subject—brought many to the rulemaking process for the first time.

As comments started pouring in to the Centers for Medicare and Medicaid Services (CMS) through the federal regulations website (www.regulations.gov), Bill Peckham, a home dialyzer, advocate, and creator of the blog “Dialysis from the sharp end of the needle” began to catalog...
CKD patients, only those most likely to be affected could be tested and treated.

With this goal in mind, Bhan and his colleagues analyzed data from 908 patients in the Accelerated Mortality on Renal Replacement (ArMORR) cohort, a nationally representative group of U.S. hemodialysis patients. The ArMORR cohort contains a variety of demographic and clinical data including medical problems and laboratory results, as well as serum and plasma samples. Data from 60 percent of the patients were used as a training set to determine potential predictors of vitamin D deficiency, and data from the other 40 percent of patients were used to validate the predictors.

Bhan’s team found that 79 percent of the study population was vitamin D deficient, with 25-hydroxyvitamin D levels less than 30 ng/mL. Black race, female sex, initiation of hemodialysis during the winter season, and hypoalbuminemia were the strongest predictors of vitamin D deficiency. In the validation set, hypoalbuminemia and initiation of hemodialysis during winter increased the likelihood of vitamin D deficiency in black females (from 90 percent to 100 percent), black males (from 85 percent to 100 percent), white females (from 82 percent to 94 percent), and white males (from 66 percent to 92 percent).

The presence of hypoalbuminemia, particularly in females and black males, may reduce the need to measure 25-hydroxyvitamin D in patients initiating dialysis between October and March, the authors suggest. Because testing is much more costly than treatment, empiric therapy with a nutritional form of vitamin D such as ergocalciferol could be considered for these individuals. The authors noted that additional studies should be done to validate their findings.

### Biological clues revealed

The research not only identifies which hemodialysis patients are at the highest risk of vitamin D deficiency, but also provides some potential biological explanations. The link between hypoalbuminemia and the deficiency suggests that at-risk patients excrete large amounts of protein—perhaps including vitamin D binding protein—in their urine. The loss of vitamin D binding protein, the main carrier of vitamin D, would inevitably cause the loss of vitamin D as well.

### Earlier studies

Earlier studies showed that patients on dialysis have an impaired ability to generate vitamin D from sun exposure. But the association between initiating hemodialysis during the winter season and vitamin D deficiency found in Bhan’s study suggests that skin-based production of the vitamin is important even in patients with ESRD.

While this study identified clinical factors that can be used to predict low 25-hydroxyvitamin D levels, it is unclear whether correcting these levels is clinically beneficial for patients with ESRD. Other experts in the field, however, stress the negative health consequences that can arise from vitamin D deficiency.

“Very low vitamin D levels can cause osteomalacia, a serious bone disease. Based on these findings, nephrologists should consider use of vitamin D supplements in most dialysis patients during winter at least,” said Daniel Coyne, MD, who was not involved with the research and is professor of medicine in the renal diseases section at Washington University School of Medicine in St. Louis.

Previous studies have shown a correlation between 25-hydroxyvitamin D levels and factors such as cardiovascular health and infection in ESRD patients. The authors noted that more research is needed to determine if supplements can have any effect on these conditions.

“The authors are correct that low vitamin D levels may just be a marker for illness, rather than mediating other adverse outcomes,” Coyne said. “We need prospective trials to prove vitamin D supplements improve patients’ health and survival.”

Study co-authors include Sherri-Ann Burnett-Bowie, MD, Jun Ye, PhD, Ravi Thadhani, MD (Massachusetts General Hospital), and Marcello Tonelli, MD (University of Alberta, Edmonton, Canada). Thadhani has received research support from Abbott Laboratories and honoraria from Abbott Laboratories and Genzyme. The other authors have no disclosures.

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**ARMORR Study Participants**

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