

New marker to predict progressive kidney failure, death

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A high level of a hormone that regulates phosphate is associated with an increased risk of kidney failure and death among chronic kidney disease (CKD) patients, according to a recent study led by researchers at the University of Miami and funded by the National Institute of Diabetes and Digestive Diseases and Kidney Diseases (NIDDK) at the National Institutes of Health. Results are in the June 15 issue of the *Journal of the American Medical Association*.

In a previous study of patients beginning hemodialysis for treatment of kidney failure, individuals with elevated blood levels of the hormone fibroblast growth factor 23 (FGF23) were found to be at nearly six times greater risk of death compared to those with lower levels. However, the hormone had not been tested in the much larger population of patients with less advanced CKD. Researchers now report that patients with earlier stage kidney disease and high FGF23 are at nearly two times higher risk of kidney failure if their baseline estimated glomerular filtration rate (eGFR) is 45 milliliters or higher, while all CKD patients are at three times higher risk of death compared to patients with lower levels of the hormone. The eGFR is a measure of kidney function.

Senior study author Myles Wolf, M.D., M.M.Sc., at the University of Miami, believes this discovery could lead to earlier diagnosis and treatment of phosphate problems. Treatment typically consists of dietary phosphate restriction and phosphate binders — medications that work like a sponge to soak up phosphate in the gut. "Since FGF23 rises before phosphate in people with early or intermediate-stage chronic kidney



disease, this hormone could be an early marker — like a road sign — pointing to patients who may benefit from early management of phosphate levels, which may help preserve kidney function and reduce deaths," he said.

Our bodies need phosphorus to build and repair bones and teeth, help cells function and maintain DNA. With fine-tuned regulation from hormones like FGF23, the kidneys help control the amount of phosphate in the blood by eliminating the excess. Elevated phosphate levels are often a consequence of advanced kidney disease or damage. But too much phosphate may also make kidney disease worse.

The findings released today are based on data from 3,879 racially diverse participants with CKD who enrolled in the NIDDK-supported, multi-center, observational Chronic Renal Insufficiency Cohort (CRIC) Study between June 2003 and September 2008. During a median follow up period of 3.5 years, 266 patients died and 410 developed kidney failure.

"The major goal of the CRIC Study is to figure out which factors might predict rapid loss of kidney function and development and worsening of heart disease in CKD patients," said Robert A. Star, M. D., director of the Division of Kidney, Urologic and Hematologic Diseases at NIDDK. "FGF23 could be the critically important puzzle piece that separates those who might have stable kidney function from those who have progressively worsening kidney disease and heart disease that requires more intensive therapy. FGF23 might work better than more traditional measures, such as protein in the urine, in certain settings."

Star added that the study of FGF23 in the CRIC Study is part of a major effort supported by the NIDDK to identify markers that can better predict the fate of patients with CKD. Further work is necessary to determine whether FGF23 actually causes death or progressively reduces



kidney function in CKD <u>patients</u>, and whether reducing FGF23 levels improves patient survival.

Next month, the NIDDK will host a meeting to discuss opportunities for randomized clinical trials to reduce the impact of CKD. For more information, visit www3.niddk.nih.gov/fund/other/... trials2011/index.htm.

An estimated 23 million American adults have CKD, and nearly 400,000 people in the United States and 2 million worldwide depend on dialysis to treat <u>kidney failure</u>. CKD costs the nation \$57.5 billion per year, or roughly 23 percent of total Medicare expenditures, and end stage renal disease carries a cost of \$39.5 billion.

Provided by National Institutes of Health

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