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Simple lab test for bone disease linked to risk of death in dialysis patients

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Among patients receiving dialysis for chronic kidney disease (CKD), high levels of alkaline phosphatase—a routinely measured laboratory marker of bone disease—may signal an increased risk of death, reports a study in the November *Journal of the American Society of Nephrology* (JASN).

"This large epidemiologic study shows, for the first time, a consistent and robust association between a high blood level of alkaline phosphatase and cardiovascular death in thousands of dialysis patients across the United States," comments Kamyar Kalantar-Zadeh, MD, of the University of California Los Angeles, one of the study authors. "If the association between alkaline phosphatase and mortality has a causal link, treatment strategies that reduce alkaline phosphatase levels may improve survival in patients with CKD, and probably in many other patients with chronic diseases and active bone disorders."

The researchers analyzed data on nearly 74,000 hemodialysis patients in DaVita dialysis clinics during a three-year period. Laboratory measurements of alkaline phosphatase level measured in a DaVita laboratory center were analyzed as a possible predictor of mortality risk. In dialysis patients, alkaline phosphatase levels are routinely measured to monitor metabolic bone disease, a common complication of CKD. However, current guidelines do not include specific recommendations or targets for serum alkaline phosphatase in CKD patients.

The results showed that patients with higher alkaline phosphatase levels

were at higher risk of death during the three-year follow-up period. After adjustment for a wide range of other risk factors, patients with alkaline phosphatase levels above the upper limit of normal (>120 IU/L) had a 25 percent increase in mortality rate.

The link between alkaline phosphatase and mortality was significant across various subgroups of dialysis patients. Surprisingly, this included patients without hepatitis or other liver diseases, which can also cause increased alkaline phosphatase levels; as well as patients who had normal serum liver function or normal nutritional status, reflected by normal serum albumin levels. In addition, patients whose alkaline phosphatase level increased during the first six months of the study were at higher risk of death over the subsequent two and one-half years.

"In dialysis patients, increased levels of alkaline phosphatase in the blood indicate a so-called high-turnover bone disease, which can happen due to hormonal imbalance in CKD," explains Dr. Kalantar-Zadeh. Previous studies have also found evidence of a link between bone disease and cardiovascular health in CKD patients. "Alkaline phosphatase has recently been shown to be associated with increased vascular calcification in experimental studies," he adds. "Our study shows the clinical manifestations of this association in real-world patients."

The study permits no conclusions as to whether high alkaline phosphatase levels are actually responsible for the increase in mortality risk. Dr. Kalantar-Zadeh concludes, "For the ultimate proof of causation, treatment trials are needed to target high bone turnover diseases to reduce serum alkaline phosphatase effectively, and then to ascertain whether these interventions can improve survival."

Source: American Society of Nephrology