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Investigating Alkaline Phosphatase Variability As A Key Predictor of All-Cause Mortality in Chronic Kidney Disease Patients: Multi-Nation Retrospective Cohort Study

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Objectives : Elevated alkaline phosphatase (ALP) levels are linked to higher mortality. However, the significance of ALP level variability on patient outcomes, particularly in chronic kidney disease (CKD), has not been well explored. This study aimed to investigate the impact of ALP variability on all-cause mortality in patients with chronic kidney disease (CKD).
Methods : This multi-ethnic, multi-center retrospective cohort study analyzed data from Taiwan and Korea from January 2001 to December 2021. Patients aged ≥18 years with CKD, defined by an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m^2, were included. ALP variability was measured using standard deviation (SD), coefficient of variance (CoV), and variance, and categorized into quartiles for analysis, with the first quartile as the reference group. A Cox-proportional hazard model, adjusted for demographic factors, comorbidities, and laboratory variables, was used to assess the impact of ALP variability on mortality.
Results : A total of 13,451 patients with CKD were included; the mean age was 63.6 ± 13.6 years; 62.2% were male. Comorbidities included hypertension (54.1%), diabetes (44.5%), and cardiovascular disease (17.0%). The mean eGFR was 36.6 ± 13.9 mL/min/1.73m^2, with 23.4% of patients in CKD stage 4 and 8.4% in stage 5. Higher ALP variability, as indicated by the top quartile in SD, CoV, and variance, was significantly associated with increased all-cause mortality (SD, aHR 1.81, 95% CI 1.61-2.04; CoV, aHR 1.49, 95% CI 1.33-1.67; Variance, aHR 1.81, 95% CI 1.61-2.04). Subgroup analysis based on comorbidities such as hypertension, diabetes, and cardiovascular disease showed that the hazard impact was consistently maintained. The impact of ALP was prominent in patients with eGFR 30-60 (aHR 2.03, 95% CI 1.76-2.34).
Conclusions : Variability in ALP levels is a significant predictor of all-cause mortality in patients with CKD, highlighting the need to monitor ALP fluctuations as part of the comprehensive risk assessment in individuals with CKD.