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Mediation effects of anemia on the impact of hypoalbuminemia in patients with chronic kidney disease

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Objectives: Anemia is common comorbidity in chronic kidney disease (CKD) patients. It is a potent but modifiable risk factor to propagate mortality in CKD patients. Hypoalbuminemia is another risk factor for the progression of CKD; we aim to evaluate the mediation effect of anemia on the impact of hypoalbuminemia.

Methods: We used two independent retrospective cohorts for CKD patients from 1997 to 2017. We excluded subjects with initial hemoglobin <11 g/dL, laboratory evaluation interval <90 days, and no estimated glomerular filtration rate (eGFR) value. Subgroup analysis was performed based on age 65, sex, eGFR 60 mL/min/1.73 m², presence of diabetes, and dyslipidemia. We performed a marginal structural model with inverse probability weighting to evaluate causality.

Results: A total of 31,973 patients were included in the study. Mean age and eGFR were 54.3 years old and 74.0 mL/min/1.73 m², respectively. There were 2,391 (7.5%) patients with hypoalbuminemia with serum albumin <3.5 g/dL. Age, female sex, hypoalbuminemia, anemia (Hb <11 mg/dL), liver disease, and lower eGFR significantly increased the risk for all-cause mortality. Also, age, female sex, hypoalbuminemia, anemia, hypertension, diabetes, and lower eGFR significantly increased the risk of end-stage kidney disease (ESKD). The mediation effect of anemia on all-cause mortality and ESKD was 28.5% (95% confidence interval [CI] 22.1-36.0) and 22.4% (95% CI 12.9-31.8), respectively. The mediation effect of anemia on all-cause mortality and ESKD was maintained irrespective of subgroup status.

Conclusions: There was a significant mediation effect of anemia on hypoalbuminemia for all-cause mortality and ESKD in patients with CKD. Assertive management of anemia additive to hypoalbuminemia is warranted in males, patients with preserved kidney function, or with comorbidities.