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The association of serum total bilirubin with renal progression in chronic kidney disease: Results from the KNOW-CKD Study

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Objectives : Bilirubin has been recognized as an important endogeneous antioxidant. Oxidative stress could be associated with renal progression. The purpose of this study was to investigate the relationship between serum bilirubin concentration and the renal progression in large-scale Korean CKD cohort patients.

Methods : Between 2011 and 2016, 2,238 CKD patients were enrolled in the KoreaN Cohort Study for Outcome in Patients With Chronic Kidney Disease (KNOW-CKD). We analyzed 2,211 participants from this cohort who had been measured for serum bilirubin levels. Renal events were defined as doubling of serum creatinine, 50% reduction in eGFR from the baseline values, or end-stage renal disease (either initiation of dialysis or kidney transplantation). A Cox proportional hazards model was applied to determine the risk factors for renal events.

Results : Patients were 53.7 ± 12.2 years old and 1,356 patients (61.3%) were male. The mean eGFR was 50.6 ± 30.3 mL/min/1.73m2 and serum bilirubin level was 0.7 ± 0.3 mg/dL. During follow-up for 36.3 ± 17.5 months, 346 (15.6%) patients reached renal outcomes. In unadjusted analyses, serum bilirubin was associated with negatively with poor renal outcomes (HR, 0.04; 95% CI 0.02-0.07; P <0.001). There was significant interaction of serum bilirubin with eGFR (interaction P = 0.037). After adjustment, the risk of developing renal outcomes was 58% lower per mg/dL increase in serum bilirubin (HR, 0.42; 95% CI, 0.20-0.88; P = 0.021) in eGFR ≤ 45ml/min/1.73m2. Serum bicarbonate was not independently associated with renal outcomes in eGFR > 45ml/min/1.73m2 (HR 0.97; 95% CI, 0.19-4.92; P = 0.973).

Conclusions : Lower serum bilirubin concentration was independently associated with adverse renal outcomes, particularly for participants with decreased kidney function. The measurement of serum bilirubin is useful for predicting kidney disease progression in patients with severe CKD.

Keywords : BIlirubin, Chronic kidney disease, renal progression