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Urine osmolality and renal outcome in patients with chronic kidney disease: The results from the KNOW-CKD

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Objectives : High urine osmolality has been known to reflect antidiuretic action of vasopressin, which may accelerate the progression of chronic kidney disease (CKD). On the contrary, low urine osmolality also correlated with faster decline of glomerular filtration rate (GFR), suggesting nephron damage from excess fluid and urinary concentrating defect. These conflicting results led us to investigate the association between urine osmolality and adverse renal outcome in a nationwide prospective cohort of CKD.

Methods : High urine osmolality has been known to reflect antidiuretic action of vasopressin, which may accelerate the progression of chronic kidney disease (CKD). On the contrary, low urine osmolality also correlated with faster decline of glomerular filtration rate (GFR), suggesting nephron damage from excess fluid and urinary concentrating defect. These conflicting results led us to investigate the association between urine osmolality and adverse renal outcome in a nationwide prospective cohort of CKD.

Results : The mean age of patients was 53.7 ± 12.3 years, and 1,241 (61.0%) patients were men. The mean eGFR was 50.5 ± 30.3 mL/min/1.73m², and 1,243 (61.1%) patients had proteinuria greater than 0.3 g/g. The mean urine osmolality was 487.8 ± 161.4 mOsm/L. Urine osmolality had a significant positive association with age, body mass index, eGFR, hemoglobin, and serum calcium concentrations, but inverse association with urinary protein-to-creatinine ratio. During a mean follow-up of 37.1 ± 18.2 months, primary outcome occurred in 321 (15.87) patients. In a multivariable Cox analysis after adjustment of confounding factors, low urine osmolality was independently associated with an increased risk of developing primary outcome (per 10 mOsm/L increase; hazard ratio [HR], 0.986; 95% confidence interval [CI], 0.973–0.999; P=0.03). The independent association between urine osmolality and renal outcome remained significant, even after adjustment of 24-hour urine volume (n=1,893; per 10 mOsm/L increase; HR=0.982; 95% CI, 0.969–0.995;

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P=0.01). Furthermore, sensitivity analyses also demonstrated that low urine osmolality was significantly associated with CKD progression in patients with polycystic kidney disease (n=338; per 10 mOsm/L increase; HR=0.960; 95% CI, 0.929–0.992; P=0.01), as well as in patients with non-polycystic kidney disease (n=1,697; per 10 mOsm/L increase; HR=0.983; 95% CI, 0.970–0.996; P=0.01).

Conclusions : Low urine osmolality was an independent risk factor for adverse renal outcome in patients with CKD. This finding suggests that osmolality may be helpful for risk stratification of disease progression in these patients.

Keywords : chronic kidney disease; renal outcome; urine osmolality