

# Glucosuria and Prognosis in Acute Kidney Injury



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Early detection and stratification of acute kidney injury (AKI) is a demanding clinical challenge. Numerous biomarkers for AKI are under investigation, and several are beginning to see clinical use, but new applications for the easily available urine dipstick are always welcome. In “Glucosuria Predicts the Severity of Puumala Hantavirus Infection,” Tietäväinen and colleagues<sup>1</sup> present data showing for the first time that glucosuria as demonstrated on urine dipstick correlates with the severity of AKI in acute hantavirus infection.

Puumala hantavirus (PUUV) causes mild hemorrhagic fever with renal involvement including proteinuria and AKI.<sup>2</sup> The authors had previously demonstrated that both albuminuria and hematuria can help predict more severe AKI in patients with PUUV,<sup>3,4</sup> and now in this issue of *KI Reports* they extend their findings to show that glucosuria at admission correlates with higher maximum creatinine during hospital stay.

By analyzing dipstick urine glucose in 195 patients presenting with acute PUUV, they found a 12% prevalence of glucosuria at admission despite normoglycemia. They determined that patients with glucosuria developed more severe AKI than nonglucosuric patients, as evidenced by the maximum recorded serum creatinine during the hospital stay. They further discovered that, compared with nonglucosuric patients, patients with glucosuria had higher maximum urea concentrations, increased albuminuria, increased urine erythrocytes, increased determinants of capillary leakage such as minimum recorded plasma albumin during hospital stay, and increased length of hospital stay. Thus, alongside correlating with more severe AKI, glucosuria in this cohort also portended a more severe overall clinical course. Remarkably, there was only a narrow window in which to observe glucosuria on dipstick, as 24 of 25 of the glucosuric patients at admission were nonglucosuric on all follow-up dipsticks.

Normoglycemic glucosuria has been well recognized as a marker of proximal tubule dysfunction, such as can occur from damage to the tubular epithelium from immunoglobulin deposition in the

setting of multiple myeloma, or from toxic exposure to drugs such as cisplatin, aminoglycosides, or tenofovir.<sup>5</sup> Generalized proximal tubule dysfunction, termed Fanconi syndrome, can develop in these circumstances and alongside glucosuria includes aminoaciduria, phosphaturia, bicarbonaturia, uricosuria, and natriuresis.

Tietäväinen and colleagues,<sup>1</sup> however, go one step further and make a connection between glucosuria and prognosis in AKI. Given that PUUV infects tubular epithelial cells and histological data show a pattern of tubulointerstitial damage following PUUV infection,<sup>2,6</sup> it was natural to suspect that PUUV infection may correlate with the severity of renal injury. Although glucosuria resulting from tubulointerstitial damage is recognized as a helpful diagnostic marker for tubular dysfunction, including in the context of acute interstitial nephritis,<sup>7</sup> a potential role for it as a prognostic marker for the severity of AKI has not yet been well worked out. In contrast, albuminuria has already been appreciated as a reliable biomarker of acute renal injury because AKI can impinge both on podocyte function and on tubular albumin reabsorption.<sup>8</sup> Accordingly, the work of Tietäväinen and colleagues<sup>1</sup> provides a helpful framework in which to further integrate the use of urine dipstick glucose into clinical practice.

Whether the findings of Tietäväinen and colleagues<sup>1</sup> can be extended to the context of AKI more generally remains an unanswered question, but certainly the use of glucosuria as a marker of AKI severity in broader patient categories deserves to be explored. The extent of tubulointerstitial insult should be expected to correlate with the degree of

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proximal tubule dysfunction, whether the cause of insult is PUUV infection or otherwise. If this is the case, it can be hypothesized that other measures of proximal tubule function, such as fractional excretion of phosphate or serum uric acid level, also could correlate with the severity of AKI and may even have greater sensitivity than glucosuria, which in this study was only transiently observed.

To conclude the reporting of the results in their paper, Tietäväinen and colleagues<sup>1</sup> outline a metric inclusive of the aggregated dipstick findings for hematuria, albuminuria, and glucosuria and find that the highest maximum plasma creatinine is observed when all 3 are present at high qualitative levels

(more than 6+/9 on the aggregated dipstick), a helpful reminder that all biomarkers, including glucosuria, are most informative when appreciated in the context of all available clinical and laboratory data.

### DISCLOSURE

The author declared no completing interests.

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