

Discussion

ABU-A 2014, uses pooled real urine specimens selected to achieve specified albumin concentrations. The Survey materials are expected to be free of artifactual matrix effects, and therefore comparisons may be made between participants' results, or method group mean or median values, and the reference method values for albumin; and between method group mean or median values for all analytes. The reference method testing for urine albumin was performed in the Renal Testing Laboratory at the Mayo Clinic in Rochester MN, using an isotope dilution, liquid chromatography, mass spectrometry method following trypsin digestion of urine proteins and calibrated with materials prepared from highly purified monomeric human albumin.

The results for all three ABU challenges show that the Dimension Vista nephelometric method had results that were in good agreement with the reference method. However, a consistent pattern of bias vs. the reference method values was observed for other methods. The All Methods/Instruments means were negatively biased: -26% at 16.3 mg/L (1.63 mg/dL), -13% at 36.5 mg/L (3.65 mg/dL) and -13% at 184 mg/L (18.4 mg/dL). Furthermore, the differences between the lowest and highest values reported were 93% at the low 16.3 mg/L (1.63 mg/dL) concentration, 54% at 36.5 mg/L (3.65 mg/dL) and 32% at 184 mg/L (18.4 mg/dL). The 36.5 mg/L (3.65 mg/dL) concentration is near a clinical decision point for moderately elevated urine albumin¹ suggesting that most routine methods, on average, underestimate the actual concentration which will contribute to misclassification of some people as having normal risk when they may have a more significant risk for early kidney damage.

A recent report from the Laboratory Working Group of the National Kidney Disease Education Program examined 332 freshly collected urine samples measured by 16 routine laboratory methods vs. the same reference method used in the ABU Survey². The report showed a variable pattern of bias with some routine methods having median biases that were positive and some negative vs. the reference method. The overall range of differences among the median values was 37-45% over the concentrations investigated. The Laboratory Working Group is collaborating with the National Institute for Standards and Technology (NIST) to develop Standard Reference Materials for urine albumin and to qualify reference measurement procedures for urine albumin at NIST and the Renal Testing Laboratory at the Mayo Clinic as part of a reference system for urine albumin to improve standardization among different routine methods^{3,4}.

Although reference method measurements were not performed for urine calcium or urine creatinine, the results can be compared among laboratories because the Survey materials were prepared from unmodified patients' urine samples. The variation in median values between different methods for urine creatinine was 9-10% and the minimum and maximum values reported by all labs differed 25-30%. Many routine methods use the same calibrator for both serum and urine creatinine measurements which may contribute to the differences for some methods. NIST recently introduced a Standard Reference Material (3667) for creatinine in frozen human urine to assist with calibration traceability for urine creatinine.

The variation in median values between different methods for urine calcium was 4-6% and the minimum and maximum values reported by all labs differed by 13-20%. There are no reference materials or reference methods specifically intended for urine calcium. However, the agreement among laboratories in the ABU Survey suggests that current calibration protocols produce reasonably good agreement among the methods represented in the Survey.

References:

1. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl.* 2013;3:1-150.
2. Bachmann LM, Nilsson G, Bruns DE, et al. State of the art for measurement of urine albumin: comparison of routine measurement procedures to isotope dilution tandem mass spectrometry. *Clin Chem.* 2014;60:471-80.
3. National Kidney Disease Education Program, Laboratory Evaluation, Urine Albumin Standardization, <http://nkdep.nih.gov/lab-evaluation/urine-albumin/urine-albumin-standardization.shtml> (accessed 8/6/14).
4. Lieske JC, Bondar O, Miller WG, et al; on behalf of the National Kidney Disease Education Program-IFCC Working Group on Standardization of Albumin in Urine (WG-SAU). A reference system for urinary albumin: current status. *Clin Chem Lab Med.* 2013;51:981-9.

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Accuracy Based Committee