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Recommendations for Reporting Low and High Values for Urine Albumin and Total Protein

To the Editor:

Urine albumin (UA)[1] and urine total protein (UP) are important biomarkers for assessing, monitoring, and determining treatment and prognosis for people with chronic kidney disease. The Laboratory Working Group of the National Kidney Disease Education Program recommended reporting UA to creatinine ratio (ACR) from a random urine collection, preferably a first morning void, because this value compares well with a 24-h UA excretion rate *(1)*. The Kidney Disease Improving Global Outcomes 2012 recommendations also include reporting the ACR and the protein to creatinine ratio (PCR) for whichever test is performed on a first morning or random urine specimen *(2)*. Clinical studies have demonstrated a strong association between prognosis and level of proteinuria *(3)*, as well as change in response to therapy *(4)*. Most national and professional organization guidelines also recommend reporting ACR or PCR when UA or UP is measured.

Clarification is needed for reporting when the measured values for UA or UP are below or above the analytical measuring range (AMR) for the measurement procedures used by a laboratory. Because quantification of UA or UP is needed for treating a patient with kidney disease, urine specimens should be diluted and measured to obtain and report a quantitative value for UA, UP, or urine creatinine when the concentration of any biomarker is above the AMR upper limit. Given the significant clinical implications of albuminuria and/or proteinuria to the assessment and management of nearly all forms of kidney disease, accurate quantitative assessment and reporting is critical.

The Laboratory Working Group of the National Kidney Disease Education Program and the IFCC Working Group for Standardization of Albumin in Urine recommend the following practices be adopted by all clinical laboratories.

1. Perform an appropriate dilution when the UA, UP, or urine creatinine value exceeds the upper limit of the AMR, and report a quantitative value for ACR or PCR, along with the concentration of UA or UP. If the manufacturer of a measurement procedure does not provide a recommended diluent or a dilution protocol, the laboratory should establish and validate a dilution protocol. The Clinical and Laboratory Standards Institute has published guidance document EP34 for extending the measuring interval through specimen dilution *(5)*.
2. In the event a technical limitation prevents diluting a specimen above a maximum reportable value, the ACR or PCR should be reported with consideration of the maximum reportable value for expressing the "greater than" indication. For example, if a measurement procedure has a maximum dilution ratio of 1:20 and an upper limit of the AMR of 200 mg/L, then the largest UA that can be reported is 4000 mg/L. For UA >4000 mg/L and assuming urine creatinine value of 1.25 g/L (11 mmol/L), the ACR is calculated and reported as >(4000/1.25) or >3200 mg albumin/g creatinine [>(4000/11) or >360 mg/mmol].
3. When the value for UA or UP is less than the lower limit of the AMR, a numeric value is not available. In this case, the ACR or PCR should be reported with consideration of the lower limit of the AMR for expressing the "less than" indication. For example, a measurement procedure has a lower limit of the AMR for UA of 5 mg/L; thus, the measured value for UA is <5 mg/L. Assuming the urine creatinine value is 0.68 g/L (6.0 mmol/L), the ACR for this example is calculated and reported as <(5/0.68) or <7 mg albumin/g creatinine [<(5/6.0) or <0.8 mg/mmol].
4. In the rare case when the urine creatinine value is less than the lower limit of its AMR, the ACR or PCR cannot be calculated, a "greater than" indication is not appropriate, and a comment such as "unable to calculate" should be used.

The instructions for use were examined for UA measurement procedures from Abbott Architect c4000, c8000, and c16000; Ortho Vitros 5600; Beckman AU680 US and international parameters, Synchron UniCell DxC 800 and Immage; Roche Cobas c 501; Siemens ADVIA, Immulite, DCA 2000+/Vantage, Dimension ExL Max, RxL Max, Vista, and BN II. Of these 13 common methods for UA, only 6 measurement procedures included a recommended diluent or information on the dilution protocol to follow for values of UA that exceed the measuring interval. We recommend that all in vitro diagnostic measurement procedures include a recommended diluent and dilution protocol in the instructions for use so that a quantitative value for UA, UP, and urine creatinine is obtained for increased concentrations.

These reporting recommendations for UA, ACR, UP, and PCR will provide caregivers with the most ap-

[1] Nonstandard abbreviations: UA, urine albumin; UP, urine total protein; ACR, urine albumin to creatinine ratio; PCR, protein to creatinine ratio; AMR, analytical measuring range.

propriate information to help treat patients with chronic kidney disease.

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