Microalbumin / Urine Albumin Update

Chronic kidney disease (defined[1] as a glomerular filtration rate below 60 ml/min/1.73 m2 and/or an albumin/creatinine ratio of > 30 mg/g) affects close to 20 million people in the United States.[2] Under the auspices of the National Kidney Disease Education Program (NKDEP), in association with the National Institutes of Health, there is a nationwide effort to draw attention to this epidemic.[3]

With respect to highlighting the prevalence of reduced GFR, increasing numbers of laboratories are reporting estimated GFR using the MDRD equation whenever serum creatinine is ordered, and efforts are underway to harmonize the measurement of serum creatinine between methods.[4]

But the measurement of urine albumin has gotten much less attention. In contrast to serum creatinine, which virtually every physician orders periodically, relatively few physicians screen with urine albumin. Even among diabetics, for whom screening is clearly recommended, the rate of screening is low.[5]

But there are many other groups of patients who should be screened, including patients with hypertension, patients who use analgesics extensively (e.g., aspirin, acetaminophen, ibuprofen), and patients with a family history of kidney disease.[5] Another problem is that many physicians believe that a dipstick protein or a urine total protein can take the place of a urine albumin, but neither test is nearly as sensitive as immunoassays for albumin.[6]

When laboratories do measure urine albumin, data from the CAP U-Survey seem to suggest that there's considerable room for improvement. The table below summarizes ***overall*** performance of participating laboratories since January 2006:

			microalbumin (mg/L)						albumin/creat ratio (mg/g)			
Specimen		median	low	high	mean	CV		median	low	high	mean	CV
2006 U-01		923.0	385.0	1300.0	925.19	9.9		1917.9	1000.0	2790.2	1921.25	12.3
2006 U-02		26.7	17.7	37.0	26.80	9.0		84.6	25.4	134.0	85.74	13.3
2006 U-05		14.0	0.0	48.0	13.05	35.9		26.3	0.0	52.7	24.86	35.4
2006 U-06		91.0	62.6	122.0	90.48	8.6		89.3	50.0	129.8	89.43	10.4
2006 U-09		26.0	9.0	38.0	26.06	10.1		51.5	26.5	74.9	52.36	12.3
2006 U-10		10.0	4.0	15.8	9.79	16.6		6.5	0.5	19.1	6.58	21.8
2007 U-01		86.0	66.0	104.0	86.19	6.2		85.1	66.0	119.4	85.55	8.3
2007 U-02		12.0	0.0	20.6	10.97	34.4		24.0	0.0	43.0	21.85	37.3
2007 U-03		11.5	3.9	16.7	11.40	15.7		7.7	2.6	12.3	7.58	16.6

As you can see, there is a great deal of between-method variability in the measurement of urine albumin, with CVs on any given sample ranging from 6% to 36%. For example, Sample U-02 in 2006 had a mean albumin of 26.8 mg/L, but values as low as 17.7 and as high as 37.0 were reported. Microalbumin/creatinine ratios on the same sample ranged from 25.4 to 134.0, clearly spanning the decision point of 30 mg/g. Similarly, even though all the ratios on 2006 Sample U-01 from 2006 are clearly pathological (ranging from 1000 to 2790), it is of some concern that the range of albumin concentrations on that sample range from 385 to 1300 mg/L.

Unfortunately, the problem is not simply a lack of harmonization of values among different methods. For example, in the current Survey, there are three individual peer groups, representing two different manufacturers, with CVs of 26.2%, 45.0%, and 77.7%.

Whether these problems are caused by calibration issues, antigen excess effects, or low concentration imprecision problems is not clear at this point. We hope to address these issues in more detail over the course of the next year. In the interim, we encourage each laboratory to look at its own assay in an effort to improve performance.

By devoting some attention to these issues, we hope to help make these analyses more reliable. The measurement of urine albumin is simply too important for the laboratory community to be content with the overall status quo.

Gary L. Horowitz, MD
Chemistry Resource Committee

References

1. National Kidney Foundation: K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. Am J Kidney Dis 2002; 39:S1-S266 (suppl 1).

2. Coresh J, Astor BC, Greene T, et al. Prevalence of chronic kidney disease and decreased kidney function in the adult US population. Am J Kidney Dis 2003;41:1-12.

3. National Kidney Disease Education Program. Available at: http://www.nkdep.nih.gov/about/index.htm Accessed: February 9, 2007.

4. Miller WG, Myers GL, Ashwood ER, et al. Creatinine measurement: state of the art in accuracy and interlaboratory harmonization. Arch Pathol Lab Med 2005;129:297-304.

5. National Kidney Disease Education Program. Available at: http://nkdep.nih.gov/professionals/chronic_kidney_disease.htm Accessed: February 9, 2007.

6. Keane WF, Eknoyan G. Proteinuria, Albuminuria, Risk, Assessment, Detection, Elimination (PARADE): a position paper of the National Kidney Foundation. Am J Kidney Dis 1999;33:1004-1010.