AVAILABILITY OF URINARY ALBUMIN MEASUREMENT IN SOUTHERN BRAZILIAN LABORATORIES

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ABSTRACT

Introduction: Diabetic kidney disease (DKD) is the leading worldwide cause of end-stage renal disease. The current recommendation is to screen for DKD by evaluating estimated glomerular filtration rate (eGFR) and measuring urinary albumin (UA) levels in a spot sample. The aim of this study was to evaluate the availability of UA measurement in Southern Brazilian laboratories.

Methods: A cross-sectional study was conducted to assess the routine use of UA in all laboratories registered in the State Pharmacy Council of Rio Grande do Sul, the southernmost state of Brazil. Data was collected by mail, e-mail, telephone, or personal interview. A sample size of at least 384 laboratories was necessary to achieve 5% precision at a 95% confidence level based on a fixed proportion of 0.5.

Results: Eight hundred and eighty laboratories currently registered in the state were invited to participate in the study; 548 (62%) answered the technical specification questionnaire. Only 306 (55%) of the 548 surveyed laboratories performed UA measurements. The laboratories were also required to provide the number of UA measurements performed per day, which ranged from less than one per week to 65 per day.

Conclusion: The availability of UA measurements is undesirably low in Southern Brazil. This demonstrates the urgent need to increase the availability of this important test. It also reveals the gap between the current guidelines and the awareness about them among health care professionals.

Keywords: Diabetes kidney disease; diabetes mellitus; urinary albumin measurement; albuminuria; diabetic nephropathy

Diabetic kidney disease (DKD) is a serious microvascular complication of diabetes mellitus (DM), and the leading worldwide cause of end-stage renal disease¹,². The early detection of DKD allows for the use of strategies to halt its development or at least delay the progression of the disease³.

The current recommendation is to screen for DKD by measuring albumin levels in a spot urine collection, which accurately replaces 24-h collections, and by evaluating serum creatinine to estimate the glomerular filtration rate (eGFR). International and national guidelines advocate the performance of these tests in patients with type 1 diabetes after 5 years of the disease, and in all patients with type 2 DM starting at diagnosis⁴,⁶.

Unfortunately, albumin measurement procedures are not readily available in all clinical laboratories, especially in low-income countries. The aim of this study was to evaluate the availability of urinary albumin (UA) measurement in Southern Brazilian laboratories.
METHODS

A survey was conducted to assess the routine use of renal function tests (UA and eGFR) in all laboratories registered in the State Pharmacy Council of Rio Grande do Sul, the southernmost state of Brazil. The state area is divided geographically into north and south regions. Our results regarding the prevalence and reporting of eGFR testing have been previously published.

This cross-sectional study started in July 2010 and ended in July 2012. The investigation was approved by the Research Ethics Committee of our institution (protocol no. 10-0129), and each laboratory agreed to participate in the survey. The variable of interest was assessed by a technical specification survey including the following questions: 1) Is urinary albumin measured in your laboratory? 2) How many albumin measurements are performed daily? Data was collected by mail, e-mail, telephone, or personal interview.

A sample size of at least 384 laboratories was necessary to achieve 5% precision at a 95% confidence level based on a fixed proportion of 0.5. Statistical analyses were performed using the Predictive Analytics Software (PASW) package, version 20.0 (Statistical Package for the Social Sciences-Professional Statistics TM, Chicago, IL, USA).

RESULTS

Of the 880 laboratories registered in the state and invited to participate in the survey, 548 (62%) answered the technical specification questionnaire (figure 1). Of these, 403/648 (62%) were located in the northern region and 145/232 (64%) were located in the southern region of the state, thus ensuring the geographic representativeness of the data collected (figure 2).

Of the 548 respondents, 306 (55%) reported to perform UA measurement at their laboratories. Of the 242 that did not measure UA, 56 sent the samples to be analyzed by an external laboratory. Thirty-four (6.9%) laboratories informed that they were only able to measure total protein concentration in urine. The laboratories were also asked about the number of albumin measurement procedures performed per day, which ranged from less than one per week to 65 per day.

DISCUSSION

Our study revealed that only half of the Southern Brazilian laboratories included in this study perform UA measurements. This alarming low rate is in contrast with the efforts of national and international DM care guidelines, which recommend the use of annual UA measurements to identify the presence of DKD. Poor accessibility to kidney function assessment has also been reported in other regions in the world. Only 33% of patients in North Africa and 30% of individuals with type 2 DM in some regions of Finland perform urinary albumin tests on a yearly basis. A recent systematic review evaluating the standards for DM care in Central and South America found that the prevalence of annual albuminuria screenings among patients with DM ranged from 1-80%, which reveals the presence of significant heterogeneity in patient care, with important barriers to healthcare. Fortunately, some countries have much higher albuminuria screening rates, such as Israel, where approximately 72.6% of patients undergo annual screening tests. In the United States, the first national initiative to establish a set of measures to assess patients with DM has been developed recently and it includes HbA1c, low-density lipoprotein, and blood pressure measurements, in addition to eye and renal examinations. Therefore, a similar national task force in this regard is clearly necessary in our country.

Albuminuria is a very simple and low-cost procedure, hardly costing more than 2-3 dollars. It is easily
adaptable to automatization, which only requires the use of routine equipment, readily available in most ordinary laboratories. Furthermore, the validity of the use of a spot urine albumin sample to detect DKD is worldwide recognized, replacing the cumbersome 24-h urine collection to screen for elevated albumin levels, additionally simplifying the procedure\textsuperscript{5}. At most, a second collection may be necessary to confirm the diagnosis due to the high coefficient of variation of this measurement\textsuperscript{15}. Therefore, there appears to be no justifiable reason for laboratories not to perform UA measurement procedures. In addition, governmental policies should implement task forces to ensure that this test is accessible to every patient. We found that some laboratories did not perform UA because the test is seldom requested (data not shown). In this regard, we identify a serious gap between the guidelines and physicians’ awareness about them, thus showing the need for further education and training of health care staff.

Albuminuria was first suggested as a marker of kidney disease in 1969, when Harry Keen and colleagues demonstrated a slight increase in UA excretion – microalbuminuria – during a glucose test in patients with DM, using a sensitive radioimmunoassay method\textsuperscript{16}. Since then, UA assessments have been extensively used as a tool to predict advanced kidney disease, cardiovascular events, and increased mortality\textsuperscript{17}. However, the reliability of UA as a diagnostic tool for DKD has been questioned by some authors, since only one-third of the patients with increased UA excretion progress to more advanced stages of the disease\textsuperscript{3}. Furthermore, approximately 25% of patients with DM have normal UA, and the diagnosis of DKD is based on reduced GFR levels only\textsuperscript{18}. Nevertheless, even though other new kidney disease biomarkers have been investigated, none of them demonstrated better diagnostic performance than albuminuria in screening for DKD\textsuperscript{19}. Recent investigations with proteomics approach suggest that this technique, in a near future, might be able to identify diabetes renal involvement earlier\textsuperscript{20}. As for now, UA has been the most extensively studied DKD marker, and is arguably the best method to screen for the condition.

The latest DKD guidelines recommend replacing the terms micro- and macroalbuminuria with the term “increased albuminuria”, since it appears to convey in a more accurate manner the idea of a continuum of risk. This idea is corroborated by our own previous findings, as well as by those of other studies, which have demonstrated that even “high-normal” albuminuria may be predictive of advanced kidney disease and mortality\textsuperscript{1-21}.

Surprisingly, it was only recently that a candidate liquid chromatography-mass spectrometry (LC-MS/MS) was developed as a reference measurement procedure to assess UA\textsuperscript{22}. Another reference measurement procedure has been developed in the Mayo Clinic Renal Function Laboratory, using trypsin digestion of whole urine followed by LC-MS/MS\textsuperscript{23}. This initiative will allow for the standardization and harmonization of UA measurements.

A limitation of our survey is that it applies only to the southernmost region of Brazil. The wealthy Southeast region (where São Paulo and Rio de Janeiro are located) could perhaps return better results. On the other hand, in the Northern region of Brazil, the poorest region of the country, an even worse scenario could be probably found.

In conclusion, in our region, the availability of urinary albumin measurements is undesirably low, indicating an urgent need to increase the availability of this simple, albeit important, procedure.

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Conflicts of Interest

The authors declare no conflicts of interest.

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