Albumin-to-Creatinine Ratio in Random Urine Samples Might Replace 24-h Urine Collections in Screening For Micro- and Macroalbuminuria in Pregnant Woman With Type 1 Diabetes

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Pre-eclampsia, a clinical syndrome of unknown etiology, is among the most common reasons for perinatal and maternal mortality (1). The incidence of pre-eclampsia in women with type 1 diabetes is considerably higher (10–20%) than in the background population (4–5%) (2). Microalbuminuria, defined as a urinary albumin excretion from 30 to 300 mg/24 h before or in early pregnancy has proven to be a good risk marker for pre-eclampsia in women with type 1 diabetes (3). However, the urinary albumin status is often not known at booking for pregnancy. The traditional method for diagnosing microalbuminuria, collection of 24-h urine samples, is cumbersome and time consuming and may be associated with collection errors and poor compliance.

The aim of this study was to determine whether measurement of the albumin-to-creatinine ratio in random urine samples can replace 24-h urine collection in screening for micro- and macroalbuminuria in pregnant women with type 1 diabetes.

RESEARCH DESIGN AND METHODS

— The study was conducted at Copenhagen University Hospital from 2000 to 2003. All women with type 1 diabetes who were admitted to our obstetric department before 14 weeks of gestation were asked to participate, and 119 women were enrolled.

The women were asked to make two 24-h urine collections and two random urine samples. The samples were collected between gestational weeks 7 and 22, since we previously have found the urinary albumin excretion to be relatively stable before week 22 in a large cohort of women with type 1 diabetes (2). In order to simplify the urine sampling as much as possible (4), no restrictions were made with respect to time of day, diet, or excercising habits.

The albumin excretion was detected using an enzyme-linked immunosorbent assay (5), and the urinary creatinine concentration was measured by standard laboratory methods (Jaffe; interassay CV 3.3%). The median values of the 24-h urine collections and of the albumin-to-creatinine ratio were calculated, and the patients were classified as having normoalbuminuria, microalbuminuria, or nephropathy accordingly.

Microalbuminuria was defined as 30–300 mg/24 h and nephropathy as values >300 mg/24 h. For albumin-to-creatinine ratio, at the definition of microalbuminuria at 2.5–25 mg/mmol for men and 3.5–25 mg/mmol for women has been suggested by Mogensen (6), but others find it generally accepted to use 30–300 μg/mg creatinine, which corresponds to 3.5–35 mg/mmol for both sexes (7). Nephropathy was defined as values >25 mg/mmol (210 μg/mg creatinine) for both sexes in this study. There is consensus that diagnosing microalbuminuria requires two of three consecutive samples within the range (8). In case the two urine samples fell into different categories, a third sample was collected and the median of all three samples determined. Of the 119 patients, 5 collected a third sample (4%).

Normally distributed variables are given as means ± SD and urinary albumin excretion as median (range). Linear regression was applied to test the correlation between medians of 24-h and random urine samples.

RESULTS

— A total of 103 (86%) women had normoalbuminuria, 7 (6%) had microalbuminuria, and 9 (8%) had macroalbuminuria/nephropathy. The age, duration of diabetes, and HbA_{1c} were 30 ± 4 years, 16 ± 7 years, and 7.6 ± 1%, with no significant differences between the groups. The urine albumin excretion (mg/24 h) was median 8 (range 0.8–30), 66 (35–196), and 677 (301–3,536), respectively. Figure 1 shows a positive correlation between the 24-h urinary albumin excretion and the albumin-to-creatinine ratio in the random urine samples ($R = 0.80$ and $P < 0.001$). A total of 15 of 16 women with an albumin excretion >30 mg/24 h had an albumin-to-creatinine ratio >2.5 mg/mmol (sensitivity 94%). All nine women with an albumin excretion >300 mg/24 h also had albumin-to-creatinine ratio >25 mg/mmol. All 103 women with an albumin excretion <30 mg/24 h had an albumin-to-creatinine ratio <2.5 mg/mmol (specificity 100%, positive predictive value 100%, negative predictive value 99%). Using 3.5 mg/mmol (30 μg/mg) as the cutoff for microalbuminuria, we found

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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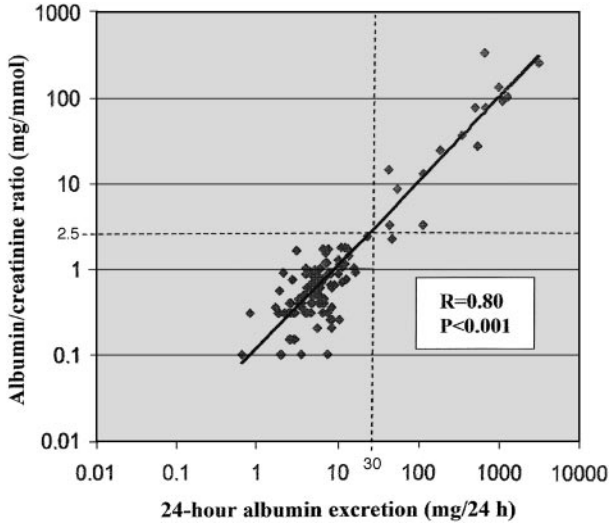

Figure 1—*Albumin-to-creatinine ratio vs. 24-h albumin excretion. Each dot represents the median of two samples. The dashed lines are the lower cutoff for microalbuminuria; 30 mg/24 h and 2.5 mg/mmol, respectively. A regression line is included;* $R = 0.80$, $P < 0.001$.

that the sensitivity was only 83%, while the specificity remained at 100% (positive predictive value 100%, negative predictive value 97%).

The day-to-day coefficient of variation was 40% for the 24-h urine collections and 49% for the random urine samples.

CONCLUSIONS — The use of random urine samples for screening for micro- and macroalbuminuria may ensure a better compliance. To better reflect the everyday clinical situation with outpatients, no restrictions were made as to the patients' diet, exercise, or time or date of sampling.

The day-to-day variation of albumin-to-creatinine ratio was slightly greater than the 24-h urine collections but did not differ from that in the nonpregnant population (9). Regardless of the method of collection, this day-to-day variation makes at least two samples necessary before taking diagnostic and therapeutic actions upon elevated values.

Earlier reports have shown good correlation between urinary albumin-to-creatinine ratio and 24-h urinary excretion in screening for microalbuminuria (10,11), and guidelines (4,7) suggest that using albumin-to-creatinine ratio is valid for screening in the nonpregnant diabetic patient. Our study is the first to demonstrate that this might also be the case in pregnant women with type 1 diabetes. However, outside pregnancy the diagnosis of microalbuminuria might still be confirmed by a 24-h urine sample. We found a cutoff value of 2.5 mg/mmol to be more successful when classifying urinary albumin excretion in random urine samples into groups of normo- and micro/macroalbuminuria in comparison with 24-h collections than the cutoff value of 3.5 mg/mmol. This is probably due to a higher creatinine clearance during pregnancy. In addition, the one patient with elevated urinary albumin excretion in the 24-h collections and normal values in the albumin-to-creatinine ratio (false-negative) turned out to have normal 24-h urinary albumin excretion in the remaining part of pregnancy. However, a much larger sample size and a harder end point would have been necessary to evaluate the exact cutoff value with acceptable precision.

We conclude that measurement of the albumin-to-creatinine ratio in two random urine samples is a highly specific and sensitive method for screening for micro- and macroalbumiuria and seems to be a good alternative to collecting 24-h urine samples in pregnant women with type 1 diabetes.

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