Ultrasonographic Determination of Residual Urine in Diabetic Subjects: Relationship to Neuropathy and Urinary Tract Infection

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The presence of residual urine was determined by postvoid bladder ultrasonography in 37 control subjects and 102 unselected insulin-dependent and non-insulin-dependent diabetic patients. Significant residual volume was detected in 19 diabetic subjects without explanation other than diabetic neurogenic bladder dysfunction in 15. The four others had prostatic hypertrophy. Excluding these four subjects, those with residual urine were slightly older than the others ($P < 0.05$), but the known duration of diabetes was increased only for the insulin-dependent group ($P < 0.05$). The presence of residual urine was strongly associated with peripheral neuropathy ($P < 0.001$). In contrast, of all the manifestations of autonomic failure studied, only impotence ($P < 0.01$) and decreased pupil motility ($P < 0.05$) were associated with residual urine. The prevalence of urinary tract infection was higher in women than in men ($P < 0.02$). This prevalence was increased in the presence of residual urine ($P < 0.02$) but only for men ($P < 0.001$). DIABETES CARE 5: 501–505, SEPTEMBER–OCTOBER 1982.

Neurogenic bladder dysfunction is a possible complication of diabetes mellitus[1,2] and is considered a manifestation of autonomic neuropathy.[3] Its presence has important implications for the treatment of diabetic patients. Diabetic cystopathy results in incomplete voiding with residual urine (RU) that (1) makes urinary glucose determination unreliable for acute appreciation of diabetic control, (2) could promote urinary tract infection, and (3) may ultimately result in hydroureteronephrosis and contribute to renal failure.[4,5]

There is need for a simple and reliable technique for detecting RU in diabetic patients. Questioning is not sufficient since patients may be asymptomatic in spite of large abnormalities at intravenous pyelogram (i.v.p.).[4] Postvoid catheterization and i.v.p. with postvoid cystogram are both invasive techniques and have undesirable features in diabetic patients. The former carries a risk of infection and the latter the risk of allergic reactions and of renal insufficiency.[6]

Vesical ultrasonography is a simple and noninvasive technique.[7,8] Its potential value for the detection of RU has been shown by Piters et al.[8] We have also used it in a large group of diabetic patients. The aims of this study were (1) to provide data on the prevalence of neurogenic bladder dysfunction, as appreciated by incomplete voiding, in diabetic patients; (2) to determine possible relationships with age, duration of diabetes, presence of peripheral neuropathy, and other manifestations of autonomic dysfunction; and (3) to confirm or refute an increased prevalence of urinary tract infection in the presence of residual urine.

SUBJECTS AND METHODS

Subjects. We studied 102 consecutive unselected diabetic patients and 37 control subjects. The diabetic group consisted of 62 insulin-dependent subjects (IDD) (38 men and 24 women aged 20–74 yr, mean 45, duration of diabetes 1–33 yr, mean 15) and 40 non-insulin-dependent patients (NIDD) (22 men and 18 women aged 30–81 yr, mean 56; known duration of diabetes 1–33 yr, mean 11). The control subjects (22 men and 15 women aged 16–86 yr, mean 44) were hospitalized patients without glycosuria or postabsorptive blood glucose levels above 5.5 mmol/L; none had neurologic abnormality at physical examination. All subjects were informed of the aims of the study.

Methods. Ultrasonographic studies were all performed with a Picker 80 L by the same investigator (D.M.) immediately after vesical voiding. This investigator did not know if the subjects did or did not have diabetes. When residual urine (RU) was detected, the largest transversal (T), longitudinal (L), and anteroposterior (AP) dimensions (cm) were determined and an index of RU was calculated as AP × L × T. The presence of hydroureteronephrosis was determined in all

subjects. In seven diabetic patients with ultrasonographic evidence of RU and in eight control subjects an i.v.p. was performed and a postvoid cystogram obtained.

The following tests were performed in all diabetic patients: (1) determination of the serum creatinine level; (2) bacteriologic examination of urine, which was collected by the midstream technique. Urinary tract infection was recognized by a bacteria count of at least 10^5/ml; (3) peripheral neuropathy was assessed clinically by finding at least one of the following: absent ankle or knee jerk, presence of lower limb dysesthesia, decreased or absent deep or superficial sensitivity of lower limbs; and (4) the presence of autonomic failure was determined by impotence, gastric atony (shown by contrast radiology), diarrhea (characterized by episodes of fecal incontinence and nocturnal bouts), loss of pupil motility, heart rate variation during deep breathing (mean of three determinations), and orthostatic hypotension (a fall of at least 30 mm Hg in systolic arterial blood pressure in the upright posture).

Data are shown as absolute or mean and extreme values (nonnormal distribution). Comparisons between groups were made using Student's *t* test and X^2 test, after logarithm transformation when necessary.

RESULTS

Determination of RU. Figure 1 shows the RU index for all subjects. Eight control subjects had evidence of a small residual volume (highest index 27). Twenty-eight diabetic patients had residual urine, with an index of over 27 in 19 (12 men and 7 women; 11 IDD and 8 NIDD). No subjects had hydroureteronephrosis. Of all the diabetic patients with RU only one (RU index 330) had a palpable painless bladder distension. Ultrasonography was repeated in 12 subjects at intervals between 3 wk and 2 mo (Figure 2). There was no significant difference between the two tests. However, residual urine was a permanent finding only when the RU index was above 30.

Intravenous pyelogram performed in the first seven diabetic patients with evidence of RU confirmed incomplete voiding (Figure 3). Bladder dimensions (T, L, and AP) were determined on the postvoid cystogram and the RU index was calculated. In these seven patients, RU indexes determined by ultrasonography or by postvoid cystogram were in good agreement (Figure 3). The i.v.p. was not performed for the others with residual urine. The eight control subjects who had i.v.p. and ultrasonography had no residual volume at either test.

Relationship of RU to age, known duration of diabetes, presence of peripheral neuropathy, and manifestations of autonomic failure (Table 1). In 15 diabetic subjects (8 men and 7 women) with RU above 30 during ultrasonography no cause other than neurogenic bladder dysfunction could be found. The last 4 patients had benign prostatic hypertrophy. Excluding these 4 subjects, diabetic subjects with RU were slightly older than the others ($P < 0.05$). Known duration of diabetes was increased only for the IDD group ($P < 0.05$). Accordingly, the prevalence of RU increased with duration of diabetes only in the IDD group (Figure 4).

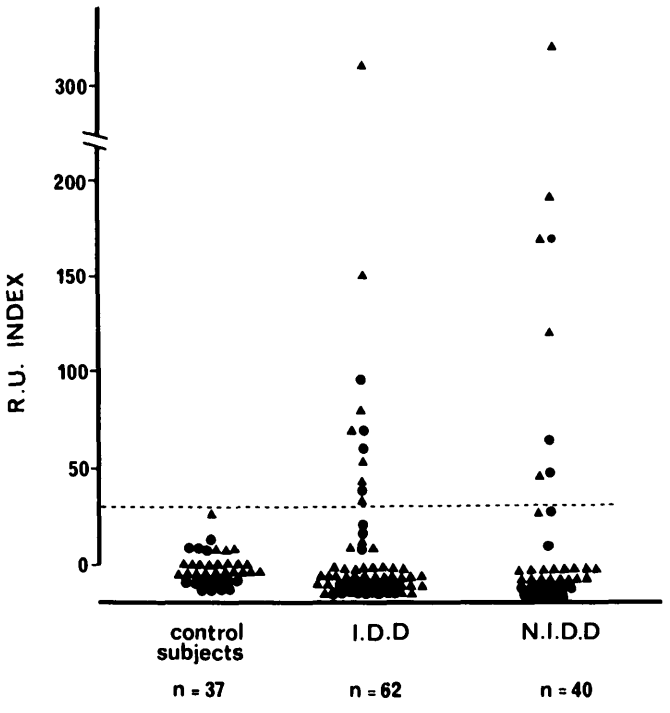

FIG. 1. RU index values for control subjects and diabetic patients (IDD: insulin-dependent patients; NIDD: non-insulin-dependent patients). ● women, ▲ men.

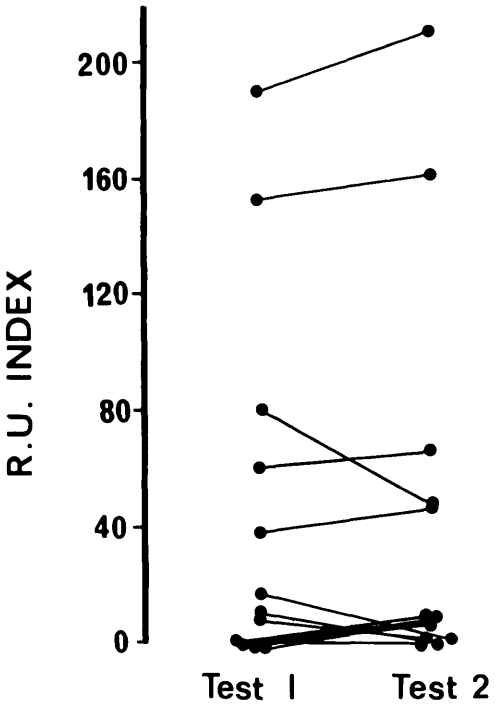

FIG. 2. Comparison of the results of two vesical ultrasonographic tests, performed at intervals between 3 wk and 2 mo, in 12 diabetic patients.

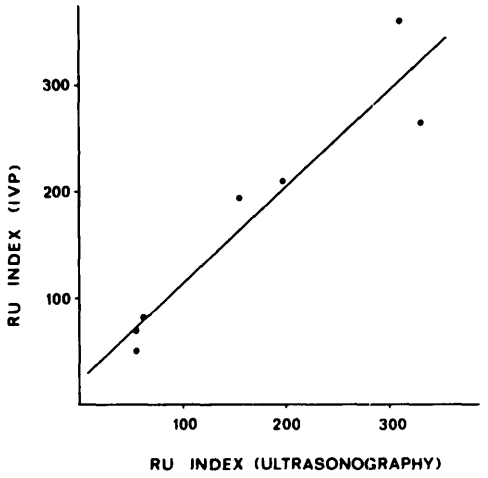

FIG. 3. Comparison of the results of the RU index calculated either by ultrasonography or with postvoid cystogram during intravenous pyelography in 7 diabetic patients.

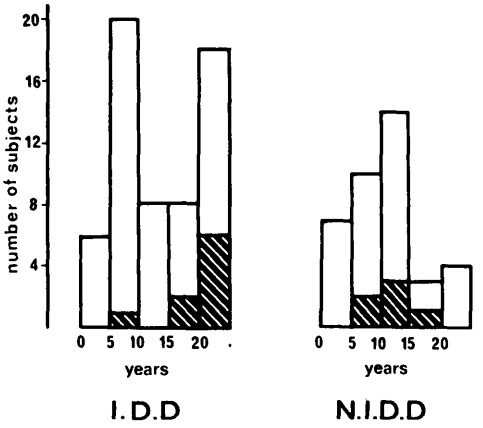

FIG. 4. Diabetic subjects with (■) and without (□) a significant RU index according to known duration of diabetes.

Always excluding the 4 subjects with prostatic hypertrophy, 36 patients (23 IDD and 13 NIDD) had clinical evidence of peripheral neuropathy. The prevalence of RU was increased in the patients with neuropathy (11/36 versus 4/62, $P < 0.001$). This difference persisted when considering only IDD (8/23 versus 1/37, $P < 0.001$), NIDD (3/13 versus 3/25, $P < 0.01$), men (7/20 versus 1/36, $P < 0.001$), or women (4/16 versus 3/26, $P < 0.01$).

Of all the manifestations of autonomic failure studied only impotence, and more weakly, decreased pupil motility were associated with neurogenic bladder. The slight decrease in beat-to-beat variation of diabetic patients with RU was not significant ($P < 0.05$). Surprisingly, orthostatic hypotension was more frequent in IDD patients without RU.

Relationship to urinary tract infection. Including all diabetic patients, bacteriuria was found in 13 subjects (6 IDD, 7 NIDD) and more frequently in women than in men (8/42 versus 5/60, $P < 0.02$). Diabetic subjects with RU had a higher prevalence of urinary infection than others (4/19 versus 9/83, $P < 0.02$). However, this difference was present only in the men (men: 3/12 versus 2/48, $P < 0.001$; women: 1/7 versus 7/35, $P > 0.20$) and persisted when men with

TABLE 1

Comparison of diabetic patients with and without significant RU with respect to age, known duration of diabetes, presence of peripheral neuropathy, and presence of symptoms of autonomic failure (data are shown as absolute values or mean and extreme values)

	Age (yr)	Duration of diabetes (yr)	Peripheral neuropathy	Heart rate variation (beat/min)	Orthostatic hypotension	Gastric atony	Diarrhea	Impotence	Decreased pupil motility
IDD (N = 60)									
With RU	52.0	21.0*	8/9†	8.2	0/9‡	0/9	1/9	4/5*	1/9
(N = 9)	35–74	7–28		0–43					
Without RU	43.8	13.2	15/51	12.4	7/51	2/51	4/51	15/31	1/51
(N = 51)	20–74	1–33		0–35					
NIDD (N = 38)									
With RU	70.2	10.2	3/6‡	6.5	2/6	0/6	0/6	2/3*	2/6
(N = 6)	66–81	5–17		0–30					
Without RU	59.0	11.2	10/32	12.2	4/32	0/32	2/32	4/17	0/32
(N = 32)	30–81	1–33		0–30					
All diabetic subjects (N = 98)									
With RU	59.5*	16.7	11/15†	7.4	2/15	0/15	1/15	6/8‡	3/15*
(N = 15)	35–81	5–28		0–43					
Without RU	49.6	12.4	25/83	12.4	11/83	2/83	6/83	19/48	1/83
(N = 83)	20–81	1–33		0–35					

* $P < 0.05$; † $P < 0.001$; ‡ $P < 0.01$.

prostatic hypertrophy were excluded (2/8 versus 2/48, $P < 0.001$). No subjects with RU had increased serum creatinine levels.

DISCUSSION

The possibility of determining the presence of RU by ultrasonography was described by Holmes[7] and next demonstrated by Piters et al.[8] We have applied this technique in a large group of control and diabetic subjects. Nearly all control subjects and most of the diabetic patients had no imaging of RU. The others had evidence of fluid within the bladder with large variations of volume. We established an arbitrary index of RU since it was not possible to calculate precisely the residual volume. However, for some of these subjects, RU volume is largely under 100 cm^3, which is considered by Piters et al.[8] as the lowest level always detectable by ultrasonography. Absolute confirmation of our results would have necessited bladder catheterization to measure exactly the residual volume. Such a technique was rejected due to its septic risk.[9] Because the results of ultrasonography were confirmed over a large index range by intravenous pyelogram in the subjects who had both tests, we think that ultrasonography is a sensitive and reliable method of detecting RU. We considered that the residual volume was significant only for an index above 30 since (1) no control subjects had an index exceeding 30, and (2) residual volume was a permanent finding only for indexes above this value.

In these conditions RU appears to be a frequent complication of both insulin- and non-insulin-dependent diabetes. We observed it in 15% of our patients. This prevalence rate is higher than the result reported by MacKay et al.[10] (1.7%). However, the prevalence of diabetic cystopathy greatly depends on the definition and the method used to assess it.[11] MacKay et al. admitted neurogenic bladder only in the presence of palpable painless bladder distension, a symptom we observed only in the patient with the highest RU index. Since this symptom only appears late in the evolution of neurogenic bladder,[4] MacKay et al. may have overlooked the diagnosis in other patients. We found that the prevalence of RU increased with the duration of diabetes in insulin-dependent but not in non-insulin-dependent subjects. The difficulty in dating exactly the onset of non-insulin-dependent diabetes could explain this discrepancy.

Although incomplete bladder voiding was more frequent in the presence of clinical peripheral neuropathy, it was also observed in its absence. Such a dissociation has also been reported for cardiac autonomic abnormalities[10] and suggests that the somatic and autonomic nervous system could be injured separately during the evolution of diabetes mellitus. Study of the association of neurogenic bladder with other manifestations of autonomic neuropathy shows results that are apparently surprising. Only impotence and decreased pupil motility were associated with RU. Orthostatic hypotension was even negatively correlated with RU in IDD patients. However, these data should be interpreted cautiously because (1) impotence,[12] decreased pupil motility,[13] diarrhea,[14] and orthostatic hypotension[15] could be due to factors other than autonomic neuropathy and (2) we only identified patients with severe abnormalities. Use of methods allowing detection of more subtle changes and precise determination of etiology could modify our results. Finally, only heart rate variation allows definite interpretation. There was no significant difference in heart rate variation between diabetic subjects with and without RU, despite a trend for lower values in the former group. In some patients neurogenic bladder was observed in the absence of cardiac autonomic neuropathy. Thus, our data do not support the conclusion of MacKay et al.,[10] who suggested that autonomic neuropathy is virtually excluded when heart rate variation is normal.

We found urinary tract infection in 12.7% of diabetic patients. This value and the difference found between men and women are similar to previously reported results.[16,17] However, contrary to Frimodt-Moller,[17] who failed to find a relationship between bacteriuria and residual urine, we found such a relationship in diabetic men, even when excluding subjects with prostatic hypertrophy.

In conclusion, the present findings confirm that vesical ultrasonography is a reliable technique for detecting residual urine. Incomplete voiding appears to be a frequent complication of diabetes mellitus, particularly in subjects with peripheral neuropathy. The presence of RU is associated with an increased prevalence of urinary tract infections in men.

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