NON-DIABETIC RENAL DISEASES IN TYPE 2 DIABETIC PATIENTS WITH RENAL INVOLVEMENT: CLINICOPATHOLOGICAL STUDY IN A SINGLE MEDICAL CENTER IN TAIWAN


Background and Objective: There has been much debate regarding non-diabetic renal diseases (NDRD) being underdiagnosed among type 2 diabetic patients with renal involvement.

Materials and Methods: We enrolled 168 type 2 diabetic patients receiving renal biopsies in our hospital from 2000 to 2009. Eighty-three patients were excluded mainly due to renal malignancies or severe kidney infections. The remaining 85 cases were retrospectively stratified according to the biopsy results into diabetic nephropathy (DN, n = 18), NDRD (n = 33), and DN plus NDRD (n = 34) groups. The major reasons for the renal biopsies being performed included acute kidney injury (AKI, including acute deterioration of chronic renal disease), overt proteinuria without retinopathy, and unexplained hematuria. Their associated clinical and laboratory findings were also analyzed.

Results: AKI events accounted for the most causes of biopsy (58.8%). In the AKI group, acute tubulointerstitial nephritis (ATIN) superimposed with DN was the most dominant (44%), followed by isolated ATIN (14%), advanced DN (12%), ATN with nephrosclerosis (4%), and variable glomerulonephritis in minor proportions. ATIN with DN also correlated with regular use of folk remedies compared with isolated DN pathologically (P < 0.05). Dominant pathological features in the atypical proteinuria and unexplained hematuria groups were DN plus membranous nephropathy and DN plus IgA nephropathy, respectively. On clinical assay, red blood cell count in urine, presence of AKI, presence of sub-nephrotic range proteinuria, and absence of retinopathy were statistically significant for NDRD (P < 0.05). In contrast, there are non-significant correlations including age, sex, onset of diabetes, duration of diabetes, serum creatinine level, serum uric acid level, HbA1C, hypertension, neuropathy, and ischemic heart disease.

Conclusions: Our study demonstrated that the above markers may predict the presence of NDRD in diabetes. Among them, use of folk remedies suggested a strong correlation with the presence of ATIN or even end-stage renal disease epidemiologically in Taiwan. (Acta Nephrologica 2010; 24: 157-166)

Key words: Type 2 diabetes mellitus (DM), non-diabetic renal diseases (NDRD), renal biopsy.

INTRODUCTION

It has been documented that renal diseases in 95% of patients with type 1 diabetes mellitus (DM) for over 10 years, particularly with the presence of diabetic retinopathy or neuropathy, are proven pathologically to be diabetic nephropathy (DN). However, in retrospective studies of type 2 diabetic populations in different series, 12-81% of the renal lesions were non-diabetic renal diseases (NDRD). The reported markers regarding NDRD include late age of onset of DM, absence of neuropathy, absence of retinopathy, and presence of other systemic diseases. Overall, it remains uncertain which clinical factors have greater value in the prediction of NDRD. The incidence and prevalence of DM have increased in recent decades. Currently, 120 million people worldwide are diabetic and this number is expected to triple in the next 30 years. The diabetes-
related medical costs are increasing, and DM has become an enormous social problem. Accordingly, the prevalence of DN is also increasing and it has become the leading cause of end-stage renal diseases (ESRD) in developed countries. According to reports of the United States Renal Data System, the number of incident patients with diabetes as their primary cause of renal failure will continue to increase, although the growth rate has slowed a little. In Taiwan, diabetes is becoming a major cause of ESRD. However, DN is not the only renal disease in diabetes. Many NDRD have been uncovered by renal biopsy. It is commonly believed that DN is hard to reverse; however, some NDRD, such as minimal change disease (MCD), mesangial proliferative glomerulonephritis (MPGN), IgA nephropathy (IgAN), and membranous nephropathy (MN), are often treatable and even remittable. The therapy and prognosis of DN and NDRD are quite different, so the differential diagnosis is of considerable importance. Previous literature has covered much of the differentiation that includes duration of diabetes, retinopathy, hematuria and other indices. However, the results are diverse, partly due to the lack of a quantified standard, and partly because they are not practicable enough for physicians with less experience. A kidney biopsy can discriminate DN from NDRD, but it is invasive and not suitable for every patient. The point in question, therefore, is that the selection criteria vary with different kidney centers, and the real frequency of NDRD is not clear due to the diversified criteria for biopsy among different kidney centers. The present study was designed to retrospectively analyze kidney biopsies on selective patients with variable conditions with the aim to discover predictive markers by comparing DN, NDRD, and DN plus NDRD, and to find features specific in our selective population compared with studies in other countries.

MATERIALS AND METHODS

Participants

Our institute has long been a medical center responsible for the national chronic kidney disease (CKD) care program in central Taiwan. In the past decade, we had retrospectively accessed our electronic database and chart records for type 2 DM patients receiving biopsies. The indications of renal biopsy of these patients, which were also the inclusion criteria of this study, were listed as follows:

**Indications of renal biopsy (Inclusion criteria)**

1. Age > 18 and < 90 years with type 2 DM.
2. Lack of known bleeding tendency, such as prolongation of prothrombin time.
3. Informed consent of patient.

*With one or more of following features:*

1. Presence of acute kidney injury (AKI in RIFLE R to F).
2. Presence of “overt proteinuria without retinopathy”.
3. Presence of “unexplained hematuria”.

The diagnosis of diabetes was made according to the criteria stated by the American Diabetes Association. The reason why we choose “AKI”, “overt proteinuria without retinopathy”, and “unexplained hematuria” as potential indicators of NDRD is that they are not common presentations of DN in the literature. The associated terms would be defined later. From January 2000 to April 2009, a total of 168 patients who visited our outpatient clinics or were hospitalized in related to our service were screened from the records and were enrolled. However, to simplify the study, biopsies done for specific purposes were not included and the exclusion criteria were as follows.

**Exclusion criteria**

1. Known NDRD existence by historical biopsy.
2. Presence of malignancy in the urinary tract.
3. Presence of severe kidney infections, such as renal abscesses.
5. Lost data or incomplete information.

There were a total of 83 patients excluded (Fig. 1). The remaining 85 cases were stratified according to the biopsy results (Table 1).

**Data collection**

NDRD were categorized according to orthodox pathological criteria. The following data were recorded prior to renal biopsy: age, sex, onset of diabetes, duration of diabetes, serum creatinine levels, glycosylated hemoglobin (HbA1c), serum uric acid level, urine microscopy and sediments, total protein amount in 24-h urine or albumin/creatinine ratio in a spot sample. Onset of diabetes was defined as the time when DM was first diagnosed. Duration of diabetes was defined as the period between the age of onset and renal biopsy. A history of ischemic heart disease was also obtained. The usage of folk remedies was determined according to chart records or electronic profiles.

**Institutional Review Board (IRB) approval**

Informed Consent Forms (ICF) provided written information to all patients and recorded the subject’s consent to take part in the biopsy procedure. The consent forms were written in Chinese at the reading level of 9th grade, and signed by the subject or the subject’s legally authorized representative.
Both inclusion and exclusion criteria are described in the main article.

Fig. 1. Flowchart of study design.

Table 1. Demographics of diabetic patients with biopsy, N = 85

<table>
<thead>
<tr>
<th></th>
<th>DN = 18</th>
<th>NDRD = 33</th>
<th>NDRD + DN = 34</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) *</td>
<td>56 ± 11.4</td>
<td>63.5±12.6</td>
<td>61.1±14.0</td>
<td>0.15</td>
</tr>
<tr>
<td>Sex (M/F) §</td>
<td>13/5</td>
<td>16/17</td>
<td>16/18</td>
<td>0.18</td>
</tr>
<tr>
<td>Onset of diabetes (age) *</td>
<td>49.4±11.3</td>
<td>56.8±12.8</td>
<td>54.5±14.5</td>
<td>0.17</td>
</tr>
<tr>
<td>Diabetes duration (years) *</td>
<td>6.7± 1.0</td>
<td>6.7± 1.5</td>
<td>6.7± 1.3</td>
<td>0.96</td>
</tr>
</tbody>
</table>

Data were expressed in mean ± SD.
* Compared by ANOVA.
§ Compared by Fisher’s exact test.
Definition of type 2 DM
The selection criteria of type 2 DM patients for this study were those defined by the American Diabetes Association (ADA),\textsuperscript{15} with the absence of a ketosis-prone state (absence of significant ketonuria and insulin treatment started at least 1 year after diagnosis).

Definition of AKI (RIFLE classes R to F)
AKI, defined as renal damage onset within 48 hrs, was clinically measured either as elevation of serum creatinine levels or reduced urine volume. The phenomenon is well defined by the RIFLE criteria as proposed by the Acute Dialysis Quality Initiative Group.\textsuperscript{18} DN is supposed to worsen renal function by 1 ml/min per month,\textsuperscript{19} and should not be compared to weak changes in monthly serum creatinine. Owing to the variable rate of renal function decline in AKI, we defined that patients must meet at least RIFLE class “R” to be classified as AKI, in which serum creatinine has increased to over 1.5 fold of the baseline or a decreased urine volume of less than 0.6 ml/kg/hr for 6 hours. In addition, acute deterioration of chronic kidney disease, also named acute chronic renal failure, which was classified as RIFLE “F” – increasing serum creatinine level over 0.5 mg/dl from baseline of 4.0 mg/dL or above, was presented in most of our patients. Nevertheless, some of our patients were biopsied at relatively low serum creatinine level (e.g., 2.5 mg/dL) although no CKDs were diagnosed prior to biopsies.

Definition of overt proteinuria without retinopathy
Patients presenting with overt proteinuria without diabetic retinopathy were considered to have “atypical proteinuria pattern of DN” and thus indicated for renal biopsy.\textsuperscript{19} The amount of proteinuria was measured either by collecting 24-hour urine for assay or by obtaining single spot urine to calculate the albumin/creatinine ratio.\textsuperscript{20} Urinary albumin excretion within the microalbuminuric range (30 mg to 300 mg/24 hr) in at least two out of three consecutive nonketotic sterile urine samples is defined as microalbuminuria.\textsuperscript{21} Overt proteinuria is defined by daily urine albumin excretion exceeding 300 mg.\textsuperscript{21} Nephrotic syndrome was diagnosed by the presence of edema, heavy proteinuria (at least 3.5 gm/day) together with a serum albumin level < 3 mg/dL.

Definition of unexplained hematuria
The presence of hematuria was defined as unexplained (i.e., exclusion of urinary tract infection, menstrual contamination, or bladder lesions) when persisting in at least two separate urine samples. It was quantified as RBC count in high-power field (HPF) microscopy. The term “microscopic hematuria” refers to, although much controversy exists, as more than 3-5 RBCs/HPF on phase contrast urine microscopy of a centrifuged urine specimen in two of three freshly voided, clean catch, midstream urine samples.\textsuperscript{22} However, most of our patients with this manifestation presented with “gross hematuria”, meaning that a higher RBC count (e.g. > 20/HPF) was detected by the time the patients participated in our study.

Definition of diabetic retinopathy
Diabetic retinopathy was diagnosed through fundoscopy by different ophthalmologists at our center. The presence of background retinopathy (microaneurysms, haemorrhages, soft exudates, hard exudates) with or without proliferative changes would make the diagnosis.\textsuperscript{23}

Definition of neuropathy
The diagnosis was made on the basis of a neurological examination with exclusion of other causes for sensorimotor polyneuropathy. As a minimum, our patients presented with decreased or loss of vibratory and pinprick sensations over the toes. Most of the syndromes were numbness and tingling of the extremities clinically, but some patients even presented with pain in a leg or foot.\textsuperscript{24} In uncertain cases, the diagnosis was made by nerve conduction studies.

Definition of hypertension
Hypertension was diagnosed when sequential diastolic blood pressure readings were 90 mmHg or higher, systolic blood pressure readings were 140 mmHg or higher, or with concurrent use of anti-hypertensive drugs.\textsuperscript{25}

Use of folk remedies
Folk remedies were defined as uneven remedies or over-the-counter Chinese herbs obtained without a prescription from a physician. Most of them were adulterants consisting of caffeine, acetaminophen, indomethacin, steroid, and hydrochlorothiazide.\textsuperscript{26} Some well-established toxins, such as plumbum and aristolochic acid, may be incidentally produced during the manufacturing procedure.\textsuperscript{27} These herbs are frequently made into pills and are commonly called “The Black Pill” in Taiwan. They are largely consumed for variable purposes, such as to eliminate osteoarthritis, headache, or even hepatitis-associated jaundice. However, many of our participants taking these remedies did not even know the names of the herbs or additional ingredients that may have been included.

Renal biopsy methods
The renal biopsy results were certified by three of our pathologists. Kidney biopsy tissues were examined by light microscopy (using hematoxylin-eosin, periodic
Acid-methenamine silver, Schiff and Congo red staining, immunofluorescence microscopy or immunoperoxidase staining (using monospecific rabbit antihuman immunoglobulin (Ig) G, IgA, IgM, C1q, C3 and fibrinogen antisera) and electron microscopy.

Morphological criteria of DN
Pathological findings of diabetic lesions included glomerular hyaline arteriosclerosis, diffuse glomerulosclerosis with or without Kimmelstiel-Wilson nodules or nodular mesangial sclerosis, exudative lesions such as “fibrin cap”, “capsular drop” or “hyaline thrombus”, microaneurysms, uniform glomerular capillary basement membrane thickening (highlighted as linear accentuation under immunofluorescence studies) and tubulointerstitial fibrosis. The diagnosis of DN was made when at least three of the above features were present.

Statistical analysis
Statistical analyses were performed using SPSS version 12.0 (SPSS Inc., Chicago, IL). Data were expressed as mean ± SD. Differences between groups were assessed by ANOVA for continuous variables and by the chi-square test for categorical variables. For smaller expected values, Fisher’s exact test was conducted to analyze the significance between categorical variables. Post-hoc analysis was calculated by Scheffé’s test, and a p value < 0.05 was considered statistically significant.

RESULTS
Participants’ profile on renal biopsy
There were a total of 85 patients studied, with 18 having isolated DN, 33 NDRD, and 34 a combination of both. All patients were ethnically Chinese. The age, sex ratio (male/female), and onset as well as duration of DM were all similar among the three groups (56 ± 11.4, 63.5 ± 12.6, and 61.1 ± 14.0 years old; P = non-significant (NS); 13/5, 16/17, and 16/18, P = NS; 49.4 ± 11.3, 56.8 ± 12.8, 54.5 ± 14.5 years, P = NS; 6.7 ± 1.0, 6.7 ± 1.5, and 6.7 ± 1.3 years, P = NS, respectively) (Table 1).

Predictors of NDRD
No differences in clinical parameters including serum creatinine, serum uric acid, HbA1C, and interestingly, proteinuria levels were observed among DN, NDRD, and NDRD plus DN patients (Table 2). Significant factors for differentiating the three groups included the amount of microscopic hematuria, presence of AKI, and presence of retinopathy (11.5 ± 8.1, 35.2 ± 9.7, and 37.6 ± 12.7, P = 0.02; 33%, 58%, and 79%, P = 0.004; 56%, 18%, and 50%, P = 0.007, respectively).

Post-hoc analysis confirmed significant differences in amount of RBC count in HPF between DN and NDRD subgroups (P = 0.047), as well as between DN and DN plus NDRD groups (P = 0.026) (Table 3). The presence of AKI was also significant between DN and DN plus NDRD (P = 0.004) groups. The presence of

<table>
<thead>
<tr>
<th>Table 2. Biochemical and clinical parameters of diabetic patients with biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>sCr (mg/dL)</td>
</tr>
<tr>
<td>Uric acid (mg/dL)</td>
</tr>
<tr>
<td>RBCs in U/A (count/HPF)</td>
</tr>
<tr>
<td>Proteinuria (g/day)</td>
</tr>
<tr>
<td>HbA1C (mg/dL)</td>
</tr>
<tr>
<td>AKI presence §</td>
</tr>
<tr>
<td>Hypertension §</td>
</tr>
<tr>
<td>Retinopathy §</td>
</tr>
<tr>
<td>Neuropathy §</td>
</tr>
<tr>
<td>Ischemic heart disease §</td>
</tr>
</tbody>
</table>

Data were expressed in mean ± SD.
* P < 0.05 indicates significant difference
§ Categorical variables were compared by Fisher’s exact test
Abbreviations: AKI: acute kidney injury; DN: diabetic nephropathy; HPF: high power field; NDRD: non-diabetic renal disease; RBC: red blood cell; sCr: serum creatinine level; U/A: urinalysis.
retinopathy indicated a significant difference between DN and NDRD groups (P = 0.007), as well as between DN plus NDRD and NDRD (P = 0.024) groups.

### Sub-nephrotic range proteinuria

The level of proteinuria among the three groups appeared to be non-significant regarding daily urine protein. There was, however, a trend that patients in the DN or DN plus NDRD group had higher daily protein loss than those with NDRD alone (mean 5.1, 5.2, and 4.3, respectively; P = 0.68). Dividing each group by the presence of sub-nephrotic range proteinuria, we found a significant difference between DN and NDRD, showing that more patients in the NDRD group had sub-nephrotic range proteinuria (P = 0.033, Table 3). Considering the bipolar distribution pattern of proteinuria in the NDRD group (data not shown), we tried to find a higher cut-off level of proteinuria as a predictor. However, the results were non-significant with a proteinuria level of 7 g/day, or even higher (data not shown).

### AKI on DN

We found a high incidence of AKI in our study population (58.8%). The subgroup analysis of AKI in the pathological results suggested that acute tubulointerstitial nephritis (ATIN) superimposed with DN accounted was the most dominant (44%), followed by isolated ATIN (14%), advanced DN (12%), ATN with nephrosclerosis (4%), ATIN with membranous nephropathy (MN) (4%), ATN with minimal change disease (MCD) (2%), ATN with nodular glomerulosclerosis (2%), ATN with DN plus MN (2%), and variable glomerulonephritis (GN) in a minor proportion (Fig 2). In addition, 36 patients presented with AKI; two patients, with overt proteinuria without retinopathy; and two patients, with unexplained hematuria with regard to the pathology results of ATIN with/without other forms of GN. A total of 40 patients (47%) were ATIN-associated in our study population. Furthermore, ATIN with DN also correlated with regular use of folk remedies compared with isolated DN pathologically (P = 0.022, Fig. 3).

### Complications of renal biopsy

There was a 5% incidence of gross hematuria post-biopsy, all of which resolved spontaneously in 48 h without blood transfusion. No other complications were experienced.

### DISCUSSION

We found a 78.8% incidence of NDRD in our selective population, which is different from the findings of other reported series.\(^{28-30}\) The fact that these identified pathologies might lead to an alteration of treatment strategies speaks for the importance of performing renal biopsies for these selected patients. On the other hand, in the past, physicians have tended to argue against performing renal biopsies for all diabetic patients presenting with renal involvement,\(^{8,29}\) as two thirds of them would only show diabetic nephropathy. Thus, it is important to be able to identify clinical markers of NDRD.

Retrospective studies of type 2 diabetic patients found that 12-81% of patients with renal involvement had non-diabetic renal diseases.\(^{4-9}\) The large variation in the reported percentages is most likely related to the selection protocol inherent in these studies. Most of these renal biopsies were performed because it was felt that the underlying lesion was not likely to be DN. The indications included severe nephrotic syndrome, hematuria, rapid decline in renal function, unexplained renal failure at presentation and absence of retinopathy. Different predictive factors were identified, with different predic-

### Table 3. Post-hoc analysis of significant parameters

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pathological group A</th>
<th>Pathological group B</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBCs in U/A (HPF)</td>
<td>DN</td>
<td>NDRD</td>
<td>0.047*</td>
</tr>
<tr>
<td>AKI §</td>
<td>DN</td>
<td>DN + NDRD</td>
<td>0.004*</td>
</tr>
<tr>
<td>Sub-nephrotic range proteinuria (&lt; 3.5 gm/day) §</td>
<td>DN</td>
<td>NDRD</td>
<td>0.031*</td>
</tr>
<tr>
<td>Retinopathy §</td>
<td>NDRD</td>
<td>DN + NDRD</td>
<td>0.024*</td>
</tr>
</tbody>
</table>

* P < 0.05 indicates significant difference

§ Categorical valuables were compared by Fisher’s exact test

Abbreviations: AKI: acute kidney injury; DN: diabetic nephropathy; NDRD: non-diabetic renal disease; RBC: red blood cell; U/A: urinalysis.
Major manifestations in our study population.

Pathological composition in patients presenting with AKI. Notably, ATN/ATIN + DN accounted for the major role.

Abbreviations: ATIN: acute tubulointerstitial nephritis; ATN: acute tubulonephritis; DN: diabetic nephropathy; GS: glomerulosclerosis; Lupus: lupus nephritis; MN: membranous nephropathy; MCD: minimal change disease; Myeloma: myeloma cast nephropathy; PSGN: poststreptococcal glomerulonephritis.

Fig. 2 Compositions of different pathology patterns in patients with presence of acute kidney injury
Although this finding rejects the argument that one has to investigate extensively for potentially treatable non-diabetic causes for grossly nephrotic diabetic patients, owing to the wide range of standard deviation in the NDRD group with proteinuria (4.3 ± 4.2 gm per day in our study), we suggested that very heavy proteinuria may indicate the presence of NDRD. We tried but failed to find a significant higher cut-off level of proteinuria in our limited-population study.

The absence of diabetic retinopathy or neuropathy has been demonstrated previously to be associated with the presence of NDRD. Our findings support retinopathy as a sequela of DN (P=0.006). In addition, Lipkin et al. found no such correlation with neuropathy in a prospective study. We also demonstrated no correlation between NDRD and the incidence of neuropathy. Thus, we believe that we cannot predict NDRD in these patients from the absence of neuropathy. Our finding that the level of renal function could not predict NDRD is in agreement with that of other reports.

IgAN is the most common GN worldwide, accounting for 29.7% of all adult GN. Even so, we witnessed a lower than usual proportion of IgAN among our population with NDRD. Since we adopted in this study the same criteria for selecting patients for renal biopsy as for any non-diabetic patient presenting with proteinuria, we believe that this seeming under-representation might suggest an etiological link between the two entities. It would be tempting to speculate an increased immune complex deposition in the presence of hyperfiltration, intraglomerular hypertension, as well as an alteration of charge by glycated proteins in diabetes. However, while there are reported cases of the co-existence of IgAN and DN, it has also been observed that these patients have a similar renal outcomes and clinical features when compared with patients having isolated DN. Thus, whether there exists a causal relationship between the two glomerulopathies remains unclear.

Accordingly, a well-established clinical course of DN is typically characterized by slow, silent, yet progressive proteinuria with initial hyperfiltration following relentless decline of the glomerular filtration rate. This process may take many years as a sequence from normoalbuminuria to microalbuminuria, followed by overt proteinuria and finally, nephrotic range proteinuria. Thus, patients who presented with sudden accelerated nephrotic syndrome, often massive, developed in previously smooth course (with normoalbuminuria or only mild microalbuminuria) should be, at least in part, suggestive of another nephrotic NDRD involvement (especially MCD or MN). Because most of our subjects are elderly with long duration of DM and with advanced CKD (Table 1), their DN (if any) were also advanced, producing more nephrosis or even nephrotic

![Renal biopsy results](image)

The statistics were analyzed by Fisher’s exact test. P value < 0.05 indicates significant difference between groups. Abbreviations: ATIN: acute tubulointerstitial nephritis; DN: isolated diabetic nephropathy; GN: glomerulonephritis.

**Fig. 3 Use of folk remedies among patients with presence of AKI in association with different pathology patterns**
syndrome, which render them difficult to be differentiated from nephrotic NDRD (although their urine protein electrophoresis profiles may be different). This may be another reason why we could not obtain a significant P value among high proteinuria level of each groups (DN, NDRD). We supposed, however, that these settings should be differentiable during early phase of DN, while proteinuria produced by DN per se, was less than that by nephrotic NDRD. On the contrary it may be reasonable to suppose an exhibit of NDRD (especially ATIN or nephritic GN, such as IgAN, rapid progressive GN) among an elderly study population with long-term diabetes and impaired renal function yet presenting with only little proteinuria (probably combined with unexplained hematuria). As our study clearly stated, on an average of 6 years after manifestation of type 2 diabetes among the elderly, NDRD produced significantly sub-nephrotic range proteinuria compared with isolated DN (Table 3). However, owing to the heterogeneous compositions of type 2 DM patients, a high level of proteinuria may not be a reliable marker of NDRD.

Lin et al. have recently studied selective renal biopsies in type 2 diabetes in a single medical center in north Taiwan, and found an ATIN prevalence exceeding 46% among all patients presenting with NDRD (with/without DN). This result is relatively high in comparison with published data from other countries, which show that ATIN accounts for 3-18% of the NDRD population with diabetes. Their data are similar to ours (47%), and may explain at least in part the etiologic of the high prevalence of acute deterioration of diabetic renal function in Taiwan. Another study regarding nutrition and health of 1740 Taiwanese adults revealed that Chinese herbal therapy is independently and positively associated with CKD. Intake of traditional Chinese herbal medicines is very popular in Taiwan, and some ingredients in Chinese herbs are erroneously considered natural and harmless. This may be the reason why these herbs are available over-the-counter. Use of folk remedies, as reported in previous studies and in ours, suggests a strong correlation with presence of ATIN or even ESRD epidemiologically in Taiwan.

CONCLUSION

Our results indicate that NDRD cannot be distinguished from DN by age of onset and duration of DM, serum creatinine level, or absence of neuropathy. RBC count in urine, presence of AKI, presence of non-nephrotic range proteinuria, and absence of retinopathy are statistically significant markers for NDRD. We also found that use of folk remedies tends to produce ATIN in diabetic patients, suggesting that the habit of taking such remedies plays a crucial role in the pathogenesis of the high prevalence of ESRD in Taiwan.

REFERENCES


