Non-Diabetic Glomerular Disease in Type II DM: 10 Years Experience

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Background: *The nature of renal damage in patients with type II diabetes remains unclear.*
Objective: *To analyze the renal histopathology in type II diabetes who underwent renal biopsy at Siriraj Hospital, renal unit over 10 year period.*
Material and Method: *The clinical and biochemical data in 54 patients with Type II DM, atypical cases of DN, were subjected to renal biopsy and analyzed retrospectively.*
Results: *Ten out of fifty-four type II diabetic patients (18.5%) were diagnosed non-diabetic nephropathy (NDN); there were 4 patients with membranous GN, 3 patients with crescentic GN1 patient of MPGN type I, 1 patient with renal change from hypertension and 1 patient with IgMN. The most important factor that had statistically significant was nephritis urine sediment (NDN: DN 40% vs. 4.5%), However 60% of NDN had no nephritic urine sediment.*
Conclusion: *There was no strong predictor to differentiate DN from NDN by clinical or biochemical data. The only significant finding in NDN was nephritic urine sediment.*

Keywords: *Diabetes mellitus type 2, Diabetic nephropathies, NDN*

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In patients with type 1 diabetes mellitus for more than 10 years, diabetic nephropathy was presented in more than 95 percent, especially those with diabetic retinopathy and neuropathy which was different from DM type II. Non diabetic nephropathy (NDN) was found 12-81%[1-6]. The predictive factors were important for the clinicians to be able to make correct diagnosis without renal biopsy. In the prospective studies NDN was found 23-39%[7-9]. In other studies[10 – 12] histological lesions were shown in DM type II of diabetic nephropathy 60%, NDN 40%. There was no difference in sex, duration of DM, proteinuria, blood sugar level , blood pressure or urine sediments in both DN and NDN.

Aim of the Study

To identify NDN in DM type II who underwent renal biopsy and to find the clinical predictors among these two groups.

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Type of the study

Retrospective study approved by Ethics Committee, Faculty of Medicine Siriraj Hospital, Mahidol University.

Material and Method

During 1995-2005 , fifty four DM type II patients were subjected to renal biopsy by indication as followings: rapid onset of glomerular disease, rapid onset of renal function deterioration, nephritis urine sediments (dysmorphic Red blood cell ± Red blood cell cast), and extra renal signs/symptoms suggestive of other systemic diseases. We studied clinical characteristics and compared them with renal pathology in order to find clinical predictors of DN and NDN, including diabetic retinopathy, diabetic neuropathy and renal function.

Result

Fifty-four patients with DM type II were analyzed. There were 10 patients who presented with NDN while 44 patients had DN alone. The demographic and biochemical data are shown in Table 1.

The urine sediments of the two groups were shown in Table 2 while nephritic urine sediments were statistically significant p = 0.001.

The extra renal manifestations such as non ST elevation or ST elevation myocardial infarction, peripheral vascular disease, claudication were also analyzed as shown in Table 3.

Non-diabetic nephropathy patients had renal histopathology as followings:

4 patients - membranous GN
3 patients - primary membranous GN
1 patient - 2° from lupus nephritis
3 patients - Crescentic GN
1 patient - MPGN type 1
1 patient - Hypertensive nephrosclerosis
1 patient - IgM nephropathy

Discussion

Diabetic glomerulosclerosis alone, nodular of diffusion, was present in 60% of type II diabetes mellitus[10] while the remainder had various other nephropathies. Patients with NDN were comparable to those with DN in mean age, sex ratio, mean duration of

Table 1. The demographics and biochemical profile of DN and NDN patients

	DN (Mean ± SD)	NDN (Mean ± SD)	p-value
Age (years)	49.0 ± 12.8	57.8 ± 15.7	0.068
Duration of DM (years)	6.4 ± 4.3	7.8 ± 7.1	0.585
BUN (mg/dL)	37.6 ± 25.8	52.9 ± 41.1	0.283
Cr (mg/dL)	3.0 ± 2.3	4.7 ± 5.1	0.329
Albumin (g/dL)	2.5 ± 0.8	2.7 ± 0.9	0.426
FBS (mg/dL)	186.3 ± 109.2	171.5 ± 49.3	0.679
HbA1C (%)	7.5 ± 1.9	7.5 ± 1.4	0.992
Cholesterol (mg/dL)	288.1 ± 164.5	251.2 ± 99.9	0.500
Triglyceride (mg/dL)	229.5 ± 159.2	222.4 ± 116.8	0.894
Na (mmol/L)	137.6 ± 4.9	135.9 ± 3.6	0.301
K (mmol/L)	3.9 ± 0.7	3.6 ± 0.9	0.270
Cl (mmol/L)	106.0 ± 6.9	106.0 ± 4.7	0.977
HCO_3 (mmol/L)	22.4 ± 4.9	20.7 ± 5.3	0.325
Ccr (ml/min)	33.3 ± 23.6	34.9 ± 32.8	0.850
Proteinuria (g/day)	7.0 ± 5.4	6.4 ± 5.5	0.769

DN = diabetic nephropathy
NDN = nondiabetic nephropathy

Table 2. Renal manifestations of both groups

	DN (cases)	NDN (cases)	Total cases	p-value
Nephrotic syndrome	35	5	40	0.103
Nephritic urine sediment	2	4	6	0.001*
Nephritis/nephrotic syndrome	9	1	10	0.667
Asymptomaticproteinuria/hematuria	1	1	2	0.339

DN = diabetic nephropathy
NDN = nondiabetic nephropathy
Nephritis = glomerular hematuria (red cell cast)
Hematuria = non glomerular hematuria

Table 3. Extrarenal manifestations of both groups

	DN	NDN	Total	p-value
DR	25	2	27	0.076
Peripheral neuropathy	13	1	14	0.263
STEMI	0	0	0	-
NSTEMI	1	0	1	1
Unstable angina	0	0	0	-
PVD, intermittent claudication	1	0	1	1
PVD, claudication	1	1	1	0.339

STEMI = ST-elevated myocardial infarction
NSTEMI = non ST-elevated myocardial infarction
PVD = peripheral vascular disease = peripheral vascular diseases are caused by structural changes in the blood vessels, such as inflammation and tissue damage. Peripheral artery disease is an example. It's caused by fatty buildups in arteries that block normal blood fl
DR = diabetic retinopathy is a damage to the retina caused by complications of diabetes mellitus that may be diagnosed by examining the retinal image taken by a digital fundus camera
Peripheral neuropathy = the term for damage to nerves of the peripheral nervous system, which may be caused either by diseases of the nerve or from the side-effects of systemic illness

DM, proteinuria > 3 gm/day, rapidly progressive renal failure and mean creatinine clearance. However, patients with NDN had less frequent diabetic retinopathy and peripheral neuropathy. Interestingly, DR was present in 67% of type II DM, in 50% of combined renal lesions and in only 10% of NDN. A type II DM without DR had approximately 50% chance of having a NDN.

In this result, we found NDN 18.5% in type II DM patients. The provisional diagnosis of these patients before renal biopsy was mostly NDN. However, the renal pathology showed mostly DN at 81.48%. The only clinical predictors of these two groups were that DN had higher proteinuria (7.05 gm/d vs. 6.48 gm/d) but this was not statistically significant.

The trend of long-term complications, such as DR or diabetic neuropathy, was found more often in DN than NDN but was not statistically significant. The only significant marker was nephritic urine sediments which were of higher statistical significant in NDN group than DN. However, we found 60% of NDN patients without nephritic urine sediments.

Conclusion

The results of this study suggest that in type II DM the possibility of NDN cannot be accurately predicted by the absence of DR or neuropathy, or by any special symptoms or signs. Therefore we recommend an individual physician's judgment of renal biopsy in type II DM to identify those patients with a treatable lesion and for better determining the renal outcome.

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พยาธิสภาพเนื้อไตในผู้ป่วยไทยที่เป็นเบาหวานชนิดที่ 2

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ภูมิหลัง: *โรคไตในผู้ป่วยเบาหวานชนิดที่ 2 พบได้ทั้งที่เกิดจากเบาหวานเอง และโรคไตชนิดอื่น ๆ ปัจจุบันยังไม่มีปัจจัยที่บอกได้ชัดเจนล่วงหน้าว่าผู้ป่วยรายใดจะมีโรคไตเป็นแบบไหน*

วัตถุประสงค์: *เพื่อวิเคราะห์ข้อมูลทางคลินิก และผลการตรวจพยาธิสภาพชิ้นเนื้อไตในผู้ป่วยเบาหวานชนิดที่ 2 และหาปัจจัยที่อาจบอกได้ล่วงหน้าว่าผู้ป่วยจะเป็นโรคไตชนิดเบาหวานเอง หรือ จากสาเหตุอื่น*

วัสดุและวิธีการ: *เป็นการศึกษาย้อนหลังเวชระเบียนผู้ป่วยเบาหวานชนิดที่ 2 จำนวน 54 ราย ที่นำมาทำ renal biopsy เนื่องจากผู้ป่วยไม่เป็น typical case ของ DN ตามข้อบ่งชี้ renal biopsy ดังนี้ rapid onset of glomerular disease, rapid onset of renal function deterioration, nephritis urine sediments, and extrarenal signs/symptoms suggestive of other systemic diseases ตั้งแต่ปี พ.ศ. 2538 ถึง พ.ศ. 2548 รวม 10 ปีเพื่อดูผลการตรวจทางคลินิก ผลทางห้องปฏิบัติการ และผลตรวจชิ้นเนื้อไต*

ผลการศึกษา: *ผู้ป่วยเบาหวานชนิดที่ 2 จำนวน 54 ราย มี 44 ราย (81.5%) ซึ่งพยาธิสภาพแสดงว่าเกิดจากเบาหวานโดยตรง คือ เป็น diabetic nephropathy อีก 10 ราย (18.5%) มีพยาธิสภาพทางไตจากสาเหตุอื่นได้แก่ membranous nephropathy 4 ราย crescentic GN 3 ราย, membranoproliferative GN type I 1 ราย, โรคไตจากความดันโลหิตสูง 1 ราย และ IgMN 1 ราย ปัจจัยที่ช่วยแยกระหว่าง DN และ NDN ได้แก่ตะกอนปัสสาวะ ที่มีเม็ดเลือดแดงชนิดเนไฟรติก มี 40% ในขณะที่โรคไตจาก DN พบ 4.5% p = 0.001 อาการแสดงทางตา หรือ neuropathy ไม่พบความแตกต่างทางสถิติทั้ง 2 กลุ่ม แม้ว่าจะมีแนวโน้มว่าพบมากในกลุ่ม DN ก็ตาม*

สรุป: *ปัจจัยที่ใช้ในการแยก DN ออกจาก NDN ที่สำคัญทางสถิติก็คือตะกอนปัสสาวะที่มีลักษณะเม็ดเลือดแดงเป็น nephritis คือมี dysmorphic red blood cell+/-red blood cell cast เท่านั้น ไม่แยกโดยอาการทางคลินิกอื่น ๆ ซึ่งไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติ*