

A Clinico Histopathological Study to Identify Non Diabetic Renal Disease in PTS of Type 2 DM with Renal Involvement

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Abstract

Background: Both diabetic nephropathy (DN) and nondiabetic renal disease (NDRD) are reported to occur in patients with type 2 diabetes mellitus (DM). The precise diagnosis of the type of nephropathy has obvious clinical, therapeutic and prognostic implication.

Aim: The aim of our study was to find out the frequency of nondiabetic kidney diseases in patients of type 2 DM with renal involvement.

Methodology: Sixty-five type 2 diabetic patients with renal involvement were included in the study. Percutaneous renal biopsy was carried in these sixty-five patients after informed consent.

Results: There was a preponderance of males (66.2%) and majority of the patients were in the age group of 41-60 years. Duration of diabetes ranged between 3 months to 30 years. The indications for renal biopsy were nephrotic syndrome 35 (53.8%), 8(12.3%) rapidly worsening renal functions, 7(10.7%) significant renal failure with normal or insignificant proteinuria at presentation, 5 (7.6%) microscopic haematuria, 10(15.3%) proteinuria in the absence of diabetic retinopathy. Renal biopsy in 65 cases revealed: isolated diabetic nephropathy in 44(67.7%), NDRD in 7(10.8%) and 12(18.5%) patients had NDRD superimposed on diabetic nephropathy. Nondiabetic glomerular disease in our patients include Membranous glomerulonephritis, IgA Nephropathy, Endocapillary Glomerulonephritis. Interstitial Nephritis and Acute tubular injury are predominant tubulointerstitial lesion in this study.

Conclusion: This study demonstrates presence of both glomerular and tubulointerstitial lesions unrelated to diabetes (NDRD) in type 2 diabetic patients with renal involvement.

Keywords: and tubulointerstitial, 2 diabetic patients, NDRD and Renal Disease.

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Introduction

Diabetic kidney disease is one of the major microvascular complications of diabetes

mellitus[1]. Diabetic kidney disease affects approximately 40% of patients who have

had diabetes for more than 20 years and contributing to substantial proportion of patients entering in to end stage renal failure. But diabetic patients are not immune to the renal disease other than diabetic nephropathy[1]. Instead, it may be possible that the abnormal diabetic kidney is more susceptible to different type of glomerulonephritis[1]. Renal disease other than diabetic nephropathy (nondiabetic renal disease) can occur in type 1 and type 2 diabetic patients[1]. A wide spectrum of nondiabetic renal disease (NDRD) including both glomerular and tubulointerstitial lesions are reported in patients with type 2 DM and their precise diagnosis requires histological examination[2]. The exact incidence of such NDRD is not known.¹The reported incidence of NDRD ranged from 23-54% in proteinuric type 2 DM patients[1]. Biopsy studies suggest that 25-50% of patient with type 2 diabetes has glomerular lesions unrelated to or in addition to diabetic nephropathy[1]. This wide variation in incidence of NDRD may be related to selection bias and variability in biopsy criteria for the diagnosis of nondiabetic nephropathy³. Our knowledge for clinical development and morphological basis for diabetic renal disease has augmented tremendously during the last half century[4] and during the last decade we have been able to identify at least some elements of its pathogenesis. Correct diagnosis is important for the patient since prognosis and treatment may vary according to the underlying cause[4]. If a patient suffering from DM develops clinical nephropathy (proteinuria) this may be due to following reasons[5].

- a. Diabetic nephropathy
- b. Non-diabetic renal disease superimposed on diabetic nephropathy.
- c. Non-diabetic renal disease alone.
- d. Normal renal structure.

A renal biopsy studied by light microscopy and immune fluorescence may provide the

key to correct diagnosis.⁵ Thus renal biopsy in diabetic patients may prove to be helpful in identifying an underlying NDRD for better management. The current study was done to identify the occurrence of NDRD in diabetic patients.

Objective: To find out the frequency of non diabetic renal disease in patients of type 2 DM with renal involvement.

Methods:

Patients admitted to inpatient department of General Medicine and Nephrology, Viswabharathi Medical college, India during study period (Sep 2019 to April 2022) fulfilling the inclusion and exclusion criteria have been enrolled.

Inclusion Criteria:

1. Type 2DM with impaired renal functions
2. proteinuria >300mg/day
3. microscopic haematuria
4. Casts in urine

Type 2 DM with any one of the above criteria is included in study.

Exclusion criteria:

1. Type 1 DM
2. Bilateral shrunken kidneys

The present study involved a total of 65 patients according to the inclusion and exclusion criteria.

Data for the proposed study was collected in a pre-tested proforma which included various parameters like age, sex, detailed history, hematological and biochemical parameters. The patients were investigated further according to protocol to evaluate the frequency of non diabetic kidney disease in type 2 DM patients with renal involvement.

Cases were selected from patients diagnosed to have type 2DM with renal involvement in the form of persistent proteinuria >300 mg/24 hrs, urinary sediment abnormalities in the form of haematuria, red cell casts, leukocyturia, acute nephritic syndrome and renal

insufficiency upon admission to the Department of Medicine and Nephrology.

The following data was recorded, and definitions used:

Age, age at onset and duration of diabetes, sex, serum creatinine, 24hr urinary excretion of protein, the presence or absence of retinopathy, hypertension.

Data from urinalysis included notation of haematuria, pyuria, red cell casts.

Renal Insufficiency: GFR < 90 ml/min/1.73m².

Nephrotic proteinuria: at least 3.5 gm proteinuria in 24 hours.

Retinopathy: presence of background retinopathy (microaneurysm, haemorrhage, soft and /or hard exudates) whether or not proliferative retinopathy had also developed.

Hypertension: A supine systolic pressure > 130 mm of Hg, diastolic pressure > 80 mm of Hg.

Proteinuria: A positive examination by dipstick on urinalysis (> 30 mg/dl).

Haematuria: > 3 red cells per high power field.

Pyuria: > 5 white blood cells per high power field.

Ultrasound evaluation of kidney was done in all patients.

Renal biopsy: Biopsy indications were the presence of Nephrotic syndrome, microscopic haematuria, proteinuria without retinopathy or unexplained rapid worsening of renal function. All patients underwent ultrasound-guided renal biopsy using a gauge 16 coaxial quick-core biopsy set. Written consent was obtained from

each patient prior to the procedure. Each kidney biopsy was prepared by cutting paraffin blocks at 3 um sections and staining 2 slides with periodic acid schiff, 2 slides for hematoxylin and eosin, 1 slide for Jones Methenamine sliver and one slide for trichrome. Immunoperoxidase staining was also performed routinely on all slides for IgG, IgA, IgM and C3.

Statistical Method

This is a descriptive and explorative study. The data in the proformas of all the 65 patients enrolled in the study was entered into the SPSS software. Categorical variables in the study were compared using Chi square test. P value of < 0.05 was considered to be significant.

Results:

There was a preponderance of males 66.2% and majority of the patients were in the age group of 41-60 years. Duration of diabetes ranged between 3 months to 30 years. The indications for renal biopsy were nephrotic syndrome 35 (53.8%), 8 (12.3%) rapidly worsening renal functions, 7 (10.7%) significant renal failure with normal or insignificant proteinuria at presentation, 5 (7.6%) microscopichaematuria, 10 (15.3%) proteinuria in the absence of diabetic retinopathy. Renal biopsy in 65 cases revealed (Table 2): isolated diabetic nephropathy in 44 (67.7%), NDRD in 7 (10.8%) and 12 (18.5%) patients had NDRD superimposed on diabetic nephropathy. Nondiabetic glomerular disease in our patients include (Table 3) Membranous glomerulonephritis, IgA Nephropathy, Endocapillary Glomerulonephritis. Interstitial Nephritis and Acute tubular injury are predominant tubulointerstitial lesion in this study.

Table 1:

Indications for renal biopsy	Frequency	percent
Nephrotic syndrome	35	53.8
Rapidly worsening renal parameters	8	12.3
Significant renal failure	7	10.7
Proteinuria in the absence of diabetic retinopathy	10	15.3

Microscopic haematuria	5	7.6
Total	65	100.0

Table 2: spectrum of NDRD in type 2 diabetes(n=19)

Lesions	Number	Percentage
IN superimposed on DN	6	31.55%
Isolated primary Glomerulonephritis	4	21.05%
ATI and IN superimposed on DN	4	21.05%
IN	2	10.5%
Endocapillary GN and ATI superimposed on DN	1	5.2%
Membranous GN superimposed on DN	1	5.2%
IgA+IN	1	5.2%

Table 3: Spectrum of non-diabetic glomerulopathy in type 2 diabetes(n=19)

IgA Nephropathy	2	28.5%
Endocapillary GN	1	14.2%
DN + Endocapillary GN	1	14.2%
DN + MGN	1	14.2%
MGN	2	28.5%

Discussion:

The exact incidence of NDKD is not known in type 2 diabetic patients[6]. However, reported incidence of NDKD ranged from 23-54.3% [6]. Biopsy studies suggests that 25-50% of patients with type 2 diabetes have a glomerular lesions unrelated to or in addition to diabetic nephropathy[6]. Histopathological examination of renal tissue revealed a wide spectrum of renal lesion including both diabetic and nondiabetic nephropathy in present study. We observed DN in 56(86.15%) patients of this isolated DN 44(67.7%) and 12 (18.5%) patients had NDRD superimposed on DN. In this study the frequency of non-diabetic kidney disease is 29.3% in type 2 diabetic patients. In a study done by **Amoah E, Lipkin Gw, Chihara J, Taft JL**, the prevalence of non-diabetic kidney diseases in proteinuric type 2 DM was approximately 30%[7]. Thus, our observation was similar to above studies.

A wide spectrum of non-diabetic renal disease both glomerular and tubulointerstitial were found in present study. Interstitial nephritis was superimposed on diabetic nephropathy in 6(31.55%) of patients, isolated primary

glomerulonephritis was present in 4(21.05%) patients, Acute tubular injury and Interstitial Nephritis superimposed on DN in 4(21.05%), Interstitial nephritis in 2(10.5%) of patients. Different types of non-diabetic glomerulonephritis superimposed on diabetic nephropathy have been reported in literature[9]. The various types of non-diabetic glomerular lesions observed in present study are: Membranous glomerulonephritis, Endocapillary proliferative glomerulonephritis and IgA Nephropathy. On review of literatures, similarly wide spectrum of non-diabetic glomerular diseases have been documented in type 2 diabetics[8]. Membranous GN was the most common non diabetic glomerular disease in type 2 proteinuricdiabetic patients[6]. Isolated idiopathic membranous nephropathy without diabetic glomerulosclerosis was reported in two proteinuric type 2 diabetic patients in a recent study.⁹ In our study three(4.6%) patients were found to have membranous nephropathy, two had isolated membranous nephropathy and another had membranous nephropathy superimposed on diabetic nephropathy. The most encountered NDRD in a recent Saudi

Arabian study by **M. jalalah** is membranous nephropathy, which is similar to our findings[10]. We noted two(3.07%) patients with endocapillary glomerulonephritis and two(3.07%) patients with IgA nephropathy. One of the two patients with IgA Nephropathy also had Acute Interstitial Nephritis. Sarcoid or amyloid nephropathy have also been reported in type 2 diabetics[8]. However, we have not observed lupus nephritis, sarcoid or amyloid nephropathy in our study. As with most progressive renal diseases, a prominent tubulointerstitial pathology develops paripassu with glomerular abnormalities in diabetes mellitus as well[8]. The spectrum of tubulointerstitial nephritis in non-diabetic kidney disease of our study include: acute interstitial nephritis, acute tubular injury and acute on chronic interstitial nephritis. The most common non-diabetic renal disease was acute interstitial nephritis 11(16.9%). In a study done by **Soni SS**, Interstitial Nephritis was found in 18.1% of patients[9]. In a study done by **M jalalah** interstitial nephritis was found in 12.5% of patients. Our results were similar to other studies[10].

Conclusion:

Presence of diabetic retinopathy in proteinuric type 2 diabetic patients does not always predict the nature of nephropathy. Renal biopsy is necessary for precise diagnosis of diabetic and non-diabetic renal lesions in type 2 diabetic patients with renal involvement.

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