ORIGINAL RESEARCH

Non-Diabetic Renal Disease (NDRD) in Patients with Diabetes Mellitus

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ABSTRACT

Introduction: Diabetus mellitus (DM) is most commonly associated with diabetic nephropathy (DMN) but these patients can manifest with wide spectrum of non-diabetic renal disease (NDRD). These NDRD includesboth glomerular and tubulointerstitial lesions. This differentiation helps in predicting the prognosis and management of these condition which are completely different and hence results in better care of these patients.

Materials and Methods: 70 patients with DM who underwent renal biopsy were analyzed prospectively.

Results: The mean age was 42 ± 10.2 years. Male:female-was 5:1, DMN patients had longer duration of DM compared to NDRD and combined group. 83% of study group had hypertension.Diabetic retinopathy was seen in 48% of DMN where as in 19% in NDRD.Mean creatinine was higher in NDRD compared to other group.Hematuria was seen in 61.9% of NDRD and 11.1% of DMN patient. Nephrotic range proteinuria was common in DMN when compared to NDRD group. Serum albumin was lower in DMN compared to other group. In DMN Group HBA1c was higher and hyperlipedima was more common.

Conclusion: Biopsy findings showed DMN in 42%, NDRD in 38% and 20% had combined DMN and NDRD. Chronic tubulointerstial disease was the commonest NDRD and PIGN was the commonest isolated glomerular disease, among combined disease IgA nephropathy was the commonest. Among DMN patient who clinically presented as rapidly progressive renal failure,they were in stage 111 or 1V DMN and IFTA scoring was higher in them.

Keywords: DMN-diabetic nephropathy, NDRD- non diabetic renal disease, IFTA- interstial fibrosis and tubular atropy. DR-diabetic retinopathy, NS-Nephrotic syndrome.

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INTRODUCTION

A wide spectrum of non-diabetic renal disease (NDRD) are reported in patients with DM and their precise diagnosis requires kidney biopsy.

We carried out this study to find the clinical, laboratory, and pathological features of NDRD in DM patients and also to see any significant differences in clinical profile between the NDRD and Diabetic nephropathy(DMN) groups.

MATERIALS AND METHODS

All DM(defined by the American Diabetes Association) patients who underwent renal biopsy were analyzed prospectively. Seventy patients were included in the study. Data were collected from inpatient file, monitor sheets, histopathological reports.

Inclusion Criteria

All diabetic patients in whomclinically NDRD was considered and renal biopsy were done were included in the study.

- Persistent hematuria that is >3 RBC(red blood cell /high power field) in more than three urine examination, rapidly progressive renal failure (RPRF), that is worsening of GFR over a short period not explainable in DMN.
- Sudden onset of nephrotic syndrome (NS), that is no progression from micro albuminuria, sub nephrotic proteinuria and then nephrotic proteinuria.
- Asymptomatic urinary abnormalities in the absence of diabetic retinopathy (DR), and other microvascular disease.
- Renal insufficiency of unexplained origin.
- Impaired renal function with no proteinuria.

Primary Glomerular disease	Group II (n=27)	Group III (n=14)
1. PIGN (Post infectious glomerulonephritis)	7(25.9%)	2(14.2%)
2. IgA Nephropathy	2(7.4%)	3(21.4%)
3. FSGS (Focal segmental glomerulosclerosis)	2(7.4%)	1(7.14%)
4. Membraneous glomerulopathy	2(7.4%)	2(14.2%)
5. Renal limited cresentericglomerulonepritis	2(7.4%)	2(14.2%)
Secondary glomerular disease	**Group 11**	**Group III**
6. Lupus Nephritis	1(3.7%)	0.0

Table-1: Glomerular disease

Tubulointerstitial disease	Group II	Group III
CTID	6(22.2%)	0(0%)
ATN	3(11.1%)	2(14.2%)
AIN	2(7.4%)	2(14.2%)

Table-2: Tubulo interstitial disease in NDRD isolated (group II) and combined group (group III)

- Short duration of diabetes.
- Normal serum albumin.

Exclusion Criteria

- Transplant patients and patients with lack of adequate clinical data were excluded.
- DMN was considered obvious and renal biopsy deferred If patients had a prolong history of diabetes with severe signs of multi organs involvement such as retinopathy and other microvascular diseases.

Renal biopsy was done using aautomated biopsy gun. Renal Tissue was processed for light microscopy analysis after using Hematoxylin and eosin, periodic acid schiff and Jones silver methenamine staining. Immunofluorescence was also done on these tissues. The biopsies were reported by pathologist.

Based on the biopsy findings, patients were categorized as:

- Isolated DMN [group I]
- Isolated NDRD[group II]
- NDRD with underlying DMN [group III]

Diabetic nephropathy was diagnosed by the presence of mesangialExpansion, with or without the nodular Kimmelstiel – Wilson (KW) Formation, basement membrane thickening, fibrin caps, or capsular drops and classified as per RPS Classification.[4] Vascular changes ofDiabetic nephropathy and tubule interstitial changes were also included in the pathological description.

STATISTICAL ANALYSIS

Chi-square/ Fisher Exact test has been used to infer the results.

Significant figures:

- Suggestive significance (P value: $0.05<P<0.10$)
- Moderately significant (P value: $0.01<P \leq 0.05$)
- Strongly significant (P value: $P \leq 0.01$).

The procedures followed were in accordance with the ethical standards of the institution.

RESULTS

Clinical syndromes of presentation were as follows;Acute Kidney Injury [22.9%], Chronic Kidney Disease [32.9%], Rapidly Progressive Renal Failure [11.4%], Nephritic syndrome [14.3%], Nephroticsyndrome [27.1%], Asymptomatic urinary abnormalities [12.9%] like hematuria and proteinuria without any clinical manifestation.

Indication of Renal Biopsy

In Maximum number of patient the indication for renal biopsy were persistant hematuria, normal fundus and rapid worsening of creatinine.

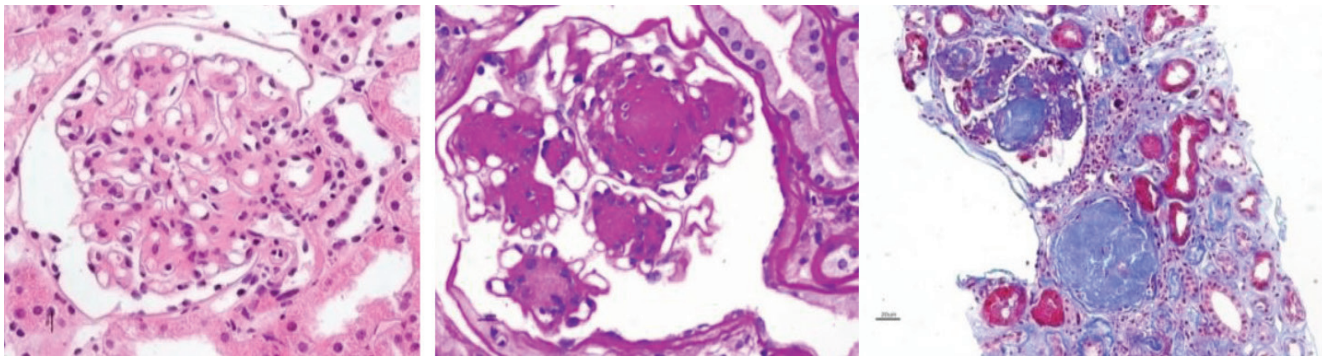
Biopsy Findings

DMN (group I) seen in 29 patients (42%), NDRD (group II) seen in 27 patients (38%), DMN and NDRD (group III) seen in 14 patients (20%).

42% patients had only diabetic nephropathy, most patients with diabetic nephropathy who had rapidly worsening renal failure and that was the indication of renal failure in these patients had advanced glomerulosclerosis, severe grade of tubular atrophy and interstial fibrosis and hyalinosis and atherosclerosis of vessels.

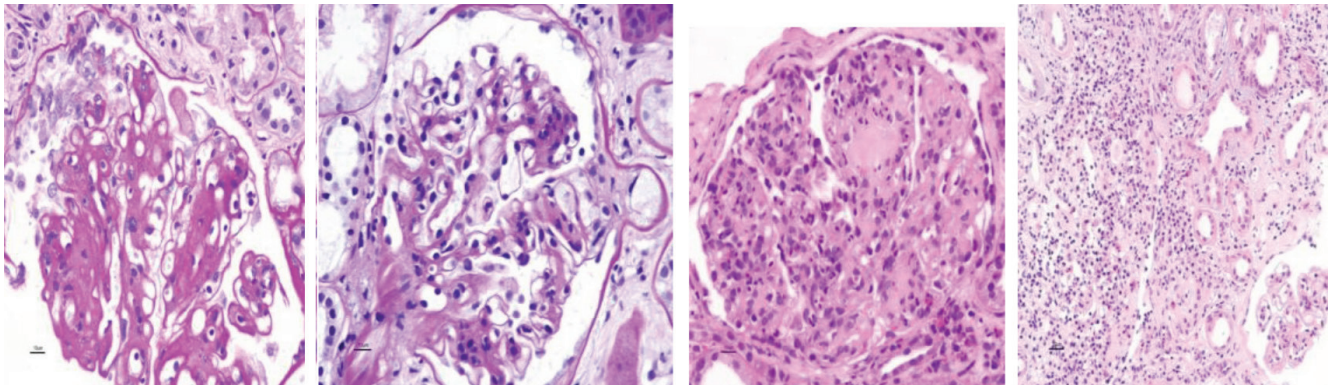
Biopsy Findings In both NDRD & Combined (DMN & NDRD)

Among the biopsy proven NDRD [27 patient], commonest glomerular disease was PIGN (25.9%), Among combined disease IgA nephropathy (21.4%) was the commonest glomerular disease Chronic tubule interstitial disease (22.2%) was the commonest Tubulo interstitial disease. Among DMN patient who clinically pre-



Class II DMN | Class III DMN with Kimmelstein wilson Class IV DMN | Class IV DMN

Figure-1: DMN



DMN with FSGS | Collapsing variant of FSGS with DMN | DMN with PIGN | DMN with acute interstitial Nephritis

Figure-2: NDRD and combined disease

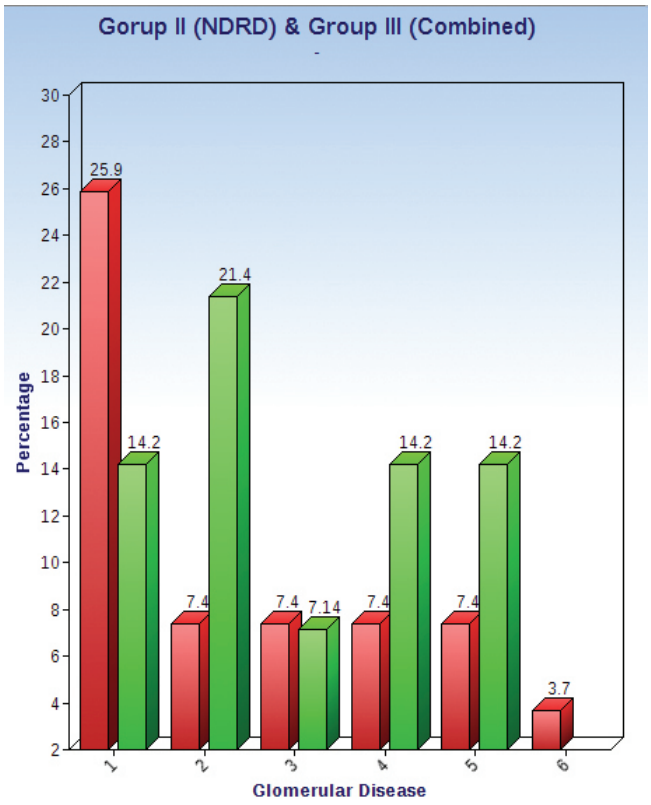


Figure-3: Glomerular Disease

sented as rapidly progressive renal failure, they were in stage III or IVand IFTA scoring was higher in them.

DISCUSSION

In this study of a selected population, the incidence of NDRD was 38%, DMN 42% AND combined was 20%. CKD, NS and AKI were the most frequent clinical presentation in our study. PIGN and CTID commonest NDRD. The Prevalence of different category of biopsyproven renal disease in diabetic patients depends on the usual prevalence of NDRD renal disease in the total population, according to the geographical area and ethnic characteristics. 58% of patients in the study had NDRD [either isolated or combined]. This study showed isolated NDRD IN 38%, this result is similar to that reported in India and other regions where incidence of isolated NDRD were less than 50%.[1,2,3] Other studies from India and also other parts of the world showed a very high incidence of NDRD. Acute interstitial nephritis was the most common NDRDshowed by Soni et al[1,4] and Prakash et al.[4] Minimal change disease was the commonest Dakshinamurthy[1] et al. IgAN was the commonest NDRD Studies from Korea and China[2]

accounted for 59% patients. Premlata et al[5] found MN as the most common pathologic change. An Iraq study reported MPGN (40%) as the commonest followed by focal segmental glomerulosclerosis (FSGS) (20%), MN (25%), MCD (10%), and amyloidosis (5%).[1] In a study from Italy where Mazzucco *et al*. analyzed kidney biopsies of 393 patients of type 2 DM observed MN (28.4%) as the most common glomerular disease followed by IgAN (22%), MCD/FSGS (20%), and PIGN (10.1%).

CKD, Nephroticsyndrome and AKI were the most frequent clinical presentation in our study. This is agreeing with majority of the published studies. From the review of literatures, it is obvious that presenting syndrome can be different. Mak *et al*. Dakshinamurthy et al[1], and Lee *et al*. observed microscopic hematuria as animportant predictor of NDRD. The frequency of hematuria in the present study is more in the NDRD 60% vs 10.%) group. Controversy exists with regards to absence of DR(diabetic retinopathy) as an indicator for NDRD. According to Pham *et al*., absence of DR is a predictor of NDRD.

This studyfocused on clinical spectrum of NDRD in DM and addressed following issues:

- Prevalence of NDRD
- Clinical features of NDRD
- Pathological lesions of NDRD
- Biochemical variation in NDRD
- Renal-retinal relationship in Type 2 DM

CONCLUSION

Kidney biopsy helps to differentiate DMN,NDRD and combined DMN and NDRD in diabetic patients, which also has prognostic and therapeutic importance.

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