

Spectrum of histopathological changes in renal biopsy of diabetic patients

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Abstract

Introduction: Diabetes mellitus is the leading cause of end stage renal disease (ESRD). The coexistence of diabetes mellitus and renal damage amplifies the risk of death in patients.

Objective: i) To determine and classify changes in renal biopsy of diabetic patients with impaired renal function
ii) To determine the relationship of these changes with deteriorating renal function.

Materials And Methods: A cross sectional study in which histopathological evaluation of 126 diabetic patients who underwent renal biopsy from Jan 2017 to June 2021 were included. On the basis of light microscopy and immunofluorescence, 3 groups of patients were defined. Group I with diabetic nephropathy alone, group II with non-diabetic renal disease (NDRD), group III with NDRD superimposed on diabetic nephropathy. Further group I was classified according to Tervaert et al, pathologic classification of diabetic

nephropathy. The histopathological changes in diabetic nephropathy were correlated with serum creatinine.

Result: 126 biopsies were performed, 96(76.1%) cases were males, mean age was 53 years. Among the 126 patients studied 92(73%) cases showed diabetic nephropathy alone, 24(19%) cases showed non-diabetic renal disease (NDRD) and 10(7.9%) cases had NDRD on top of diabetic nephropathy. In group I, 10 cases (10.8%) were class IIa, 14(15.2%) class IIb, 20 (21.7%) class III and maximum 48(52.1%) were class IV. The percentage of interstitial fibrosis with tubular atrophy and interstitial inflammation was most in class IV. Mean serum creatinine level was also significantly greater in class IV diabetic nephropathy. In group II, chronic interstitial nephritis was the most common seen in 10 cases (41.6%). In group III, focal segmental glomerulosclerosis (FSGS) was the commonest seen in 3 cases (30%).

Conclusion: Diabetic patients undergoing renal biopsy for impaired renal function constituted heterogenous group of renal damage and maximum number of patients (52.1%) had class IV diabetic nephropathy. This study emphasizes the usefulness of renal biopsy for determining the pattern of renal damage and its relationship with deteriorating renal function that would aid in better management of patients.

Novelty: This study reveals that early renal biopsy in diabetic patients can be of great significance to enable better treatment and prevent progression.

Keywords: Diabetic nephropathy, renal biopsy, non-diabetic renal disease.

Introduction

Diabetes mellitus (DM) is the leading cause of end stage renal disease (ESRD). Patients with diabetes subjected to renal biopsy may manifest diabetic nephropathy (DN) alone, DN with superimposed nondiabetic renal disease (NDRD), or NDRD alone. Differentiating between these diagnostic categories can influence patient management and prognosis. Diagnosing nondiabetic renal disease (NDRD) is especially important when it leads to a specific change in therapy.¹

Patients with DN typically show varying degrees of proteinuria and renal impairment. Because these clinical signs are frequently seen in other glomerulopathies, it is sometimes difficult to make a definitive diagnosis of DN without renal biopsy.² It has been estimated that upto one-third of diabetic patients presented with impaired renal functions are suffering from non-diabetic renal diseases, which reported to have better prognosis than diabetic nephropathy.³

We undertook this study to evaluate the morphological findings in all renal biopsies of diabetic patients

processed at our center over a period of four and a half years.

Aims And Objectives

- To determine and classify changes in renal biopsy of diabetic patients with impaired renal function.
- To determine the relationship of microscopic changes in renal biopsy with deteriorating renal function.

Study Type: Cross sectional study

Study duration: January 2017 to June 2021 (4.5 years)

No. of cases: 126

Specimen type: Renal biopsy

Source of material: 10% Formalin Fixed Paraffin embedded (FFPE) tissue blocks.

Inclusion Criteria

All renal biopsy specimens from diabetic patients with impaired renal function irrespective of their age and gender.

Exclusion Criteria

- Cases where there was inadequate sample for either HPE or DIF.
- Patients who had not given consent.

Statistical Analysis

All the categorical variables were expressed as frequency, mean, standard deviation and percentage.

Materials And Methods

On the basis of light microscopy and immunofluorescence, 3 groups of patients were defined.

Group I with diabetic nephropathy (DN) alone,

Group II with non-diabetic renal disease (NDRD),

Group III with NDRD superimposed on DN.

Further group I was classified according to Tervaert et al, pathologic classification of diabetic nephropathy. The histopathological changes in DN were correlated with serum creatinine.

Result

In this study a total of **126** renal biopsies were included. 96 cases (**76.1%**) were males and 30 (**23.8%**) were females. Male: female ratio - 3.2:1. Mean age was **54.8 ±11.1**years(34-75years)

Among the 126 patients studied, 92 cases (73%) showed DN alone. 24 cases (19%) showed non-diabetic renal disease (NDRD), 10 cases (7.9%) had NDRD superimposed on DN.

In **group I**: according to Tervaert et al, pathologic classification of diabetic nephropathy (2010), 10 cases (10.8%) were class IIa, 14(15.2%) class IIb, 20(21.7%) class III, maximum 48(52.1%) were class IV. In group I patients, mean **serum creatinine** level of 5.6 ± 3.1 mg/dl was seen in patients with class IV DN which was greater than the mean levels in class IIa (1.7mg/dl), IIb(2.4mg/dl) and class III(2.8mg/dl). Among the three groups, the highest mean **Serum creatinine** of 4.2 ± 3.2 mg/dl was seen in group III (NDRD on DN) patients. In **group II**, chronic interstitial nephritis was the most common lesion seen in 10 cases (41.6%). In **group III**, focal segmental glomerulosclerosis (FSGS) was the commonest lesion seen in 3 cases (30%).

Histological findings in renal biopsies from year 2017 to 2021

YEAR	STUDY POPULATION (n)	DIABETIC NEPHROPATHY ALONE (GROUP I)	NON-DIABETIC RENAL DISEASE (GROUP II)	MIXED (GROUP III)
2017	24	19(79.1%)	05(20.8%)	0
2018	46	29(63.1%)	15(32.6%)	02(4.3%)
2019	43	35(81.3%)	02(4.6.5%)	06(13.9%)
2020	07	05(71.4%)	0	02(28.5%)
2021	06	04(66.6%)	02(33.3%)	0

Comparison of Tissue Injury in Group I

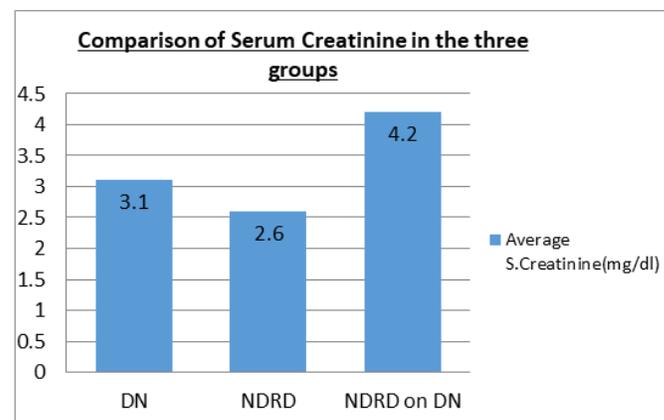
		TYPE IIa (n - 10)	TYPE IIb (n - 14)	TYPE III (n - 20)	TYPE IV (n - 48)
PERCENTAGE OF GLOMERULI SHOWING GLOBAL SCLEROSIS		10.53% ±11.9	24.4% ±15.6	36.1% ±23.6	74.9% ±16.8
INTERSTITIAL FIBROSIS AND TUBULAR ATROPHY		5.5% ±7.5	17.1% ±12.4	13.9% ±14.3	51.4% ±25.2
INFLAMMATORY CELL INFILTRATION		3.1% ±4.6	11.7% ±6.9	11% ±8.6	17.7% ±10.3
ARTERIOLAR HYALINOSIS	Score-1	2(20%)	9(64.2%)	4(20%)	4(8.3%)
	Score-2	3(30%)	4(28.5%)	15(75%)	44(91.6%)
ARTERIOSCLEROSIS	Score-1	5(50%)	13(92.8%)	15(75%)	39(81.2%)
	Score-2	0	0	2 (10%)	7(14.5%)

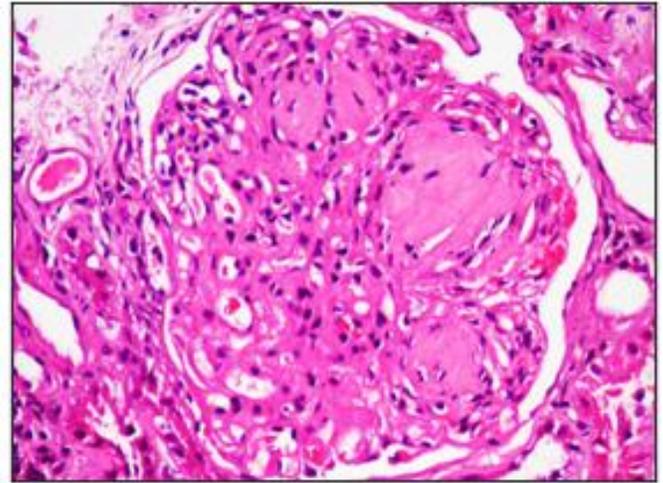
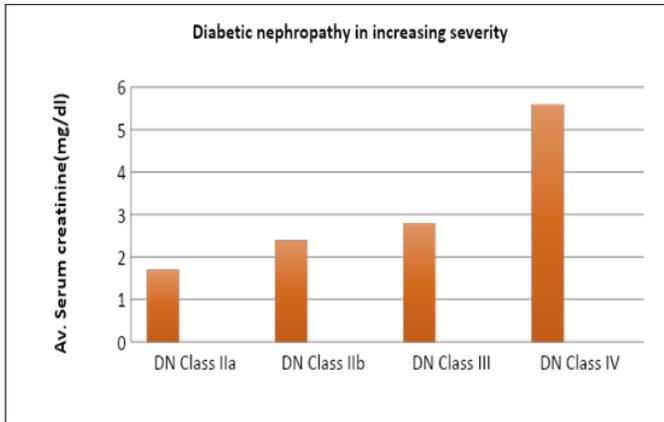
Histopathological Findings in Group II

TYPE OF NON-DIABETIC RENAL DISEASE	NUMBER OF CASES (n-24)	PERCENTAGE%
CHRONIC INTERSTITIAL NEPHRITIS	10	41.6%
MEMBRANOUS GLOMERULONEPHRITIS	06	25%
CHRONIC GLOMERULONEPHRITIS	04	16.6%
POST INFECTIOUS GLOMERULONEPHRITIS	02	8.3%
MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS	01	4%
MINIMAL CHANGE DISEASE	01	4%

Histopathological Findings in Group III

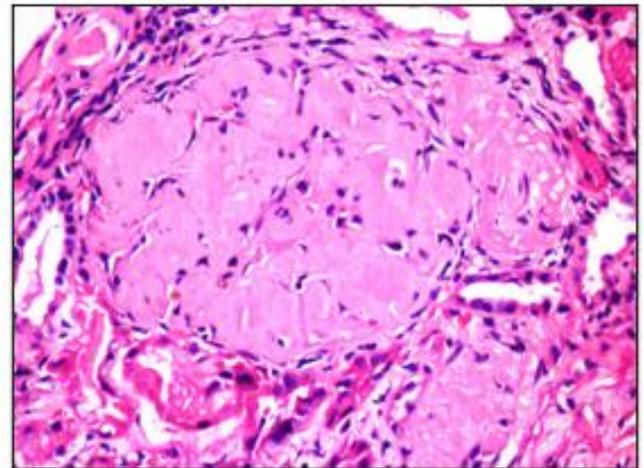
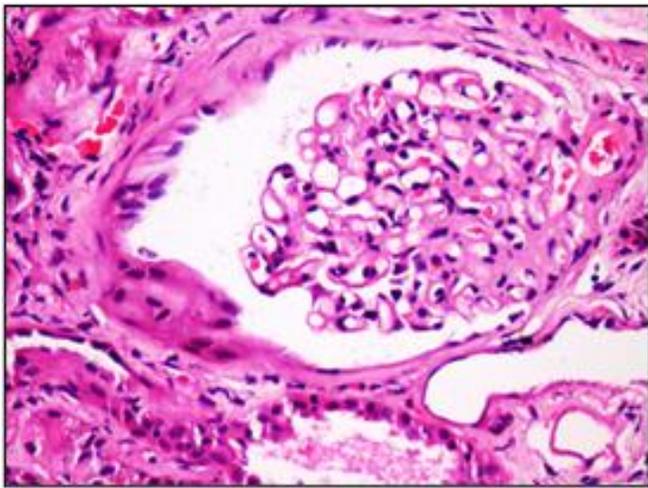
TYPE OF NON-DIABETIC RENAL DISEASE WITH DIABETIC NEPHROPATHY	NUMBER OF CASES (n-10)	PERCENTAGE%
FOCAL SEGMENTAL GLOMERULOSCLEROSIS	03	30%
CRESCENTIC GLOMERULONEPHRITIS	02	20%
MEMBRANOUS GLOMERULONEPHRITIS	02	20%
HYPERTENSIVE ARTERIOSCLEROSIS	02	20%
ACUTE TUBULAR INJURY	01	10%





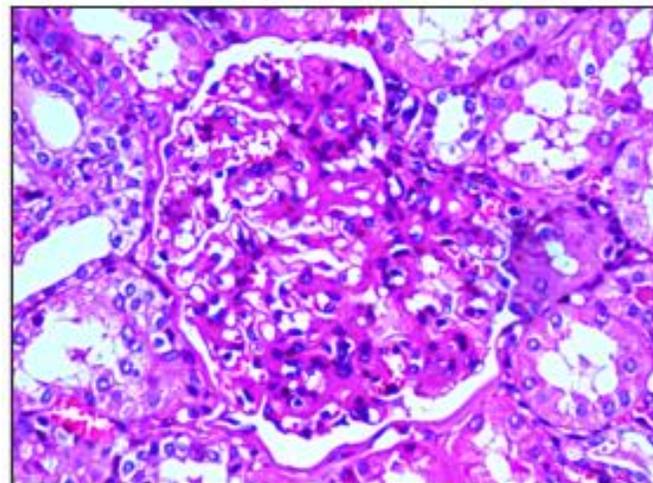
Diabetic Nephropathy Class - III

Diabetic Nephropathy Alone Group I



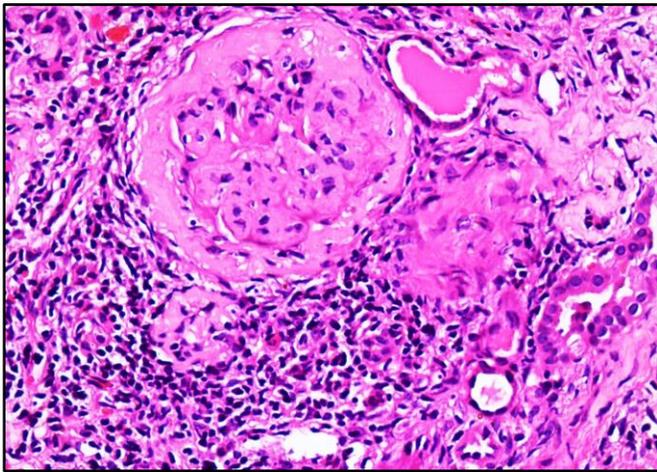
Diabetic Nephropathy Class - IV

Diabetic Nephropathy Class-II a

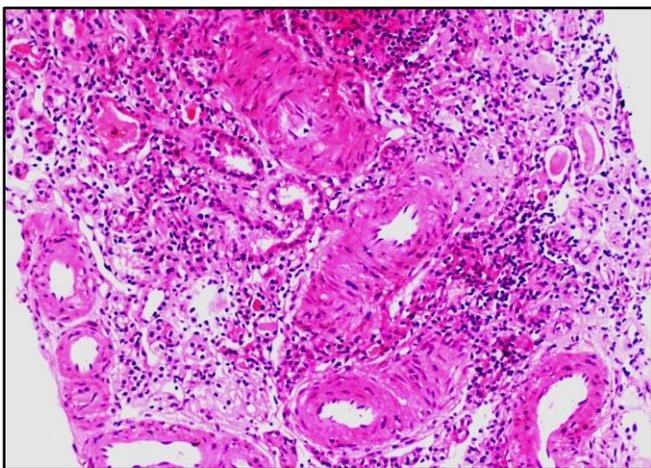


DN Class - IV With Arteriolar sclerosis And Capsular Drop

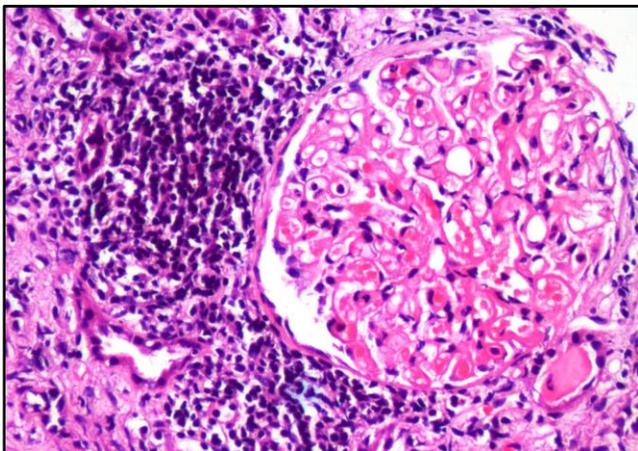
Diabetic Nephropathy Class-IIb



Non-Diabetic Renal Disease (Group II)

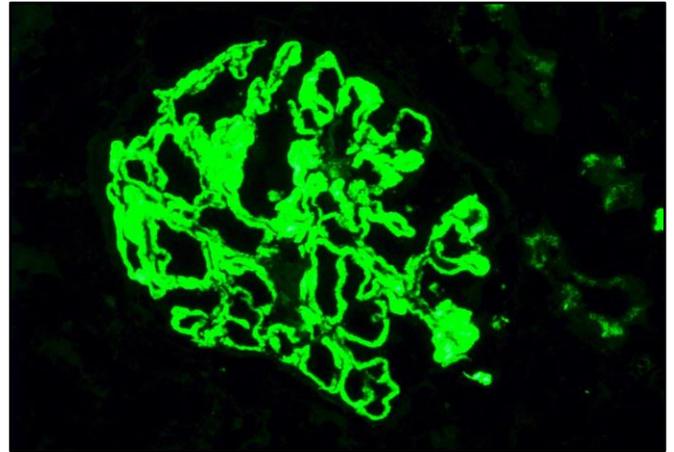


DN Class-IV With Moderate Chronic Interstitial Nephritis



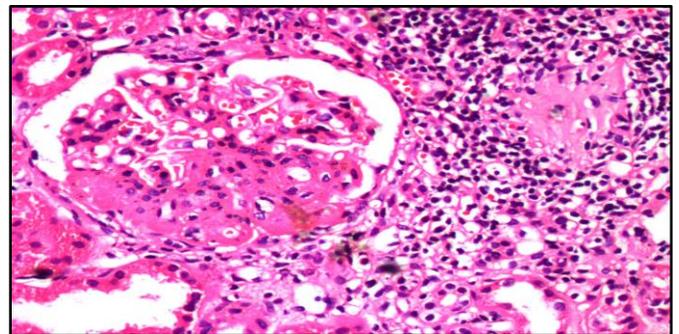
Chronic Interstitial Nephritis

Membranous Glomerulonephritis

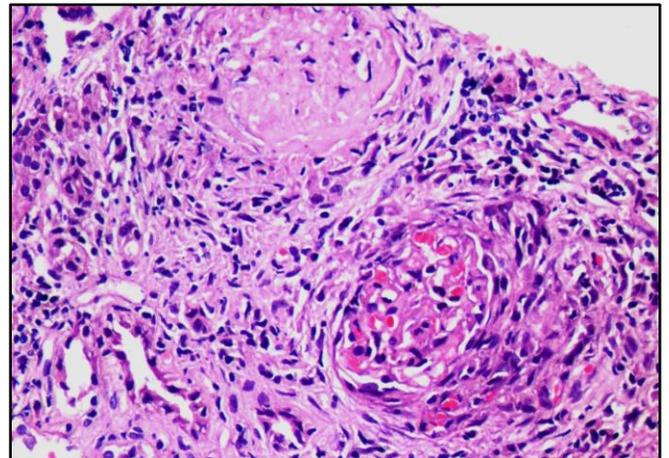


Direct Immunofluorescence Showing Fine Granular Deposits of IgG AND C3.

Non-diabetic renal disease (NDRD) on diabetic nephropathy (group III)



Focal segmental glomerulosclerosis (FSGS)



Crescentic Glomerulonephritis

Discussion

The reported frequency of NDRD in diabetics varies from 7 to 44%.⁴ IgA nephropathy was most frequent

(44%) in a study conducted in Japan,⁵ while non-diabetic glomerulopathy and Tubulo- Interstitial Nephritis (TIN) were almost in equal proportions in a research carried out in India.⁶ The present study showed that NDRD was seen in 19% of the studied diabetic population and chronic interstitial nephritis was the commonest NDRD among diabetic patients. Non-diabetic renal diseases with DGS have a significantly worse renal outcome than those without DGS.³ The most important aspect of this study is not only that NDRD was identified in a significant number of diabetic patients who underwent kidney biopsy, but also the spectrum of NDRD seen superimposed on DN (7.9%), the most common being FSGS on DN. These results are similar to a study conducted in USA, which reported FSGS (21%), the most common lesion in patients with type-II diabetes followed by MCD (15.3%).⁷

Conclusion

Renal biopsy of diabetic patients with impaired renal function constituted heterogenous group of renal damage and maximum number of patients (52.1%) had class IV DN. This study emphasizes the usefulness of renal biopsy for determining the pattern of renal damage in diabetic patients and its relationship with deteriorating renal function that would aid in better management of patients.

Thus early renal biopsy can be of great significance to enable better treatment of patients and prevent progression.

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