A Study of Prevalence of Non Diabetic Renal Disease in Patients with Diabetic Nephropathy

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Introduction
Diabetic nephropathy is one of the leading cause of ESRD. It is also one of the most significant long term complications in terms of morbidity and mortality in patients with diabetes. Furthermore, prognosis in such patients is very poor compared with patients with ESRD due to other renal diseases. Diabetic nephropathy (DN) is suspected based on the presence of proteinuria, decline in GFR and elevation of blood pressure. Renal biopsy is not routinely performed in diabetic nephropathy patients. Recently, attention has been drawn to atypical presentation of diabetic and non diabetic glomerular diseases. Renal biopsy in proteinuric patients with diabetes mellitus is to confirm/exclude non-diabetic renal disease (NDRD). There are no standardized criteria for renal biopsy in DN, therefore doing a renal biopsy for patients with DN is the based on decision of the treating nephrologist.

The prevalence of Non-diabetic renal diseases (NDRD) from various studies ranged from 23-54% in type 2 DM patients. Identification of Non-diabetic renal diseases is important as diabetic nephropathy is difficult to reverse in comparison to NDRD which when treated adequately can be reversed. Therefore, kidney biopsy may become a useful diagnostic option among proteinuric patients with diabetes mellitus.

In 2010 Research Committee of the Renal Pathology Society (RPS) developed a consensus classification combining type 1 and type 2 diabetic nephropathies by Tervaert et al. in this classification, diabetic nephropathy is divided into four hierarchical glomerular lesions with separate evaluation for interstitial and vascular lesions. However the clinical utility of this pathological classification for predicting outcomes is not established. This study aimed to evaluate the relationship between histological changes and clinical parameters in diabetic patients with renal dysfunction.

Materials and Methods
Aim of the study
• To study the prevalence of non diabetic renal disease in patients with diabetic nephropathy.
To study histopathological correlation of diabetic nephropathy with clinical parameters.

**Inclusion criteria**
- All diabetic patients with renal dysfunction admitted in the wards of Nephrology Gandhi hospital, who underwent renal biopsy during December 2013 to December 2015 were included.

**Exclusion criteria**
- Acute precipitating event for renal dysfunction
- Patients with bilateral contracted kidneys.
- Patients with contraindications for renal biopsy
- Patients unwilling for renal biopsy

The prospective study was carried out from December 2013 to December 2015 in the Department of Nephrology, Gandhi Hospital. Of 139 diabetic patients with presumed diabetic kidney disease admitted, 43 patients have contracted kidneys, 8 patients have acute precipitating event and 26 patients who were not willing for biopsy were excluded from the study. 62 patients were biopsied and their histopathology studied.

Informed consent was obtained from each patient before biopsy. Diagnosis of diabetes was made using ADA criteria for diagnosis of Diabetes 6. Detailed history with regards to type of diabetes, duration, treatment for diabetes, details of renal symptoms, micro and macro vascular complications and clinical examination was done. Fundus examination was performed by single ophthalmologist. Further evaluation viz, renal profile (blood urea, serum creatinine, serum electrolytes, complete urine examination, 24hr urinary protein) was done. eGFR was calculated by the MDRD formula in adults and Schwartz formula for children. RBS, FBS, PLBS, complete hemogram, liver function tests, CT, BT, PT, INR, and appropriate imaging and radiological investigations were done. Ultrasonographic examination was done to assess the renal size. Renal biopsy was performed in 62 patients after stabilization under ultrasound guidance with a biopsy gun (BARD gun 18 G, 22 mm, cutting edge). 2 samples were collected in all, samples were analyzed under light microscope and immunofluorescence by a single pathologist. All universal precautions were executed during the biopsy. Processed tissue was stained with hematoxylin and eosin (H & E), PAS, silver methenamine, and Masson trichrome for light microscopy. Tissue for IF was stained with fluorescent labeled antisera to IgG, IgM, IgA, C3, C1q, and Fibrinogen. The intensity was semiquantitatively scored, as 0 for negative, 1+ for present, 2+ for definite and 3+ for strongly positive. Vital parameters were monitored in the immediate post biopsy period. Renal lesions in diabetic nephropathy were classified according to “Pathologic Classification of Diabetic Nephropathy” by - Thijs W. Cohen Tervaer et al, Renal pathology society. This classification scheme is based on glomerular lesions. Patients with severe renal insufficiency were supported with either intermittent peritoneal dialysis (IPD) or hemodialysis (HD). IPD was due using rigid catheter and using 1.7% PD solution with as exchange volume of 30-50ml/kg for children and 1.5-2 liter for adults. HD was performed using 1.2 square meter hollow fibre for the duration of 4 hours with either femoral or jugular catheter of appropriate size as vascular access.

In all cases renal histopathology was analyzed in correlation with age, sex, duration of DM, Proteinuria, Fundus examination, RFT/eGFR, associated hypertension, glycemic control and need for renal replacement therapy. Fundus examination was done by single ophthalmologist by direct ophthalmoscopy in all cases and 78D/90D Slit lamp biomicroscopy where ever indicated.

Statistical analysis was performed by utilizing SPSS software. Initially frequency tables were made to estimate the frequency & percentage of each parameter analyzed. Descriptive statistics
were expressed in terms of minimum, maximum, mean & standard deviation. Logistic regression was used for the prediction of occurrence of an event. The probability of association between two discrete attributes was made by chi square test. Means of the various parameters were compared by using student t-test (for 2 groups) or by ANOVA (for more than 2 groups). P < 0.05 was considered significant.

**Proforma**

| Name | Age | Sex | Occupation |
|------|-----|-----|------------|
| IPNo | DOA | DOD |            |

**Type of diabetes:**
**Duration of diabetes:**

**Complaints & Duration**

**H/O Present illness**

- H/o oliguria
- H/o polyuria, nocturia
- H/o hematuria/pyuria/gravelluria/dysuria/frequency/urgency
- H/o obstructive symptoms
- H/o pedal edema/SOB/
- H/o Azotemia
- H/o blurring of vision/retinal surgeries/laser photocoagulation
- H/o parasthesias
- H/o recent GE/precipitating factors
- H/o usage of nephrotoxic drugs/herbal medicine intake

**Past History**

- HTN/CKD/CAD/TB/asthma/epilepsy

**Family History**

- DM/HTN/CKD/

**Menstrual & Obstetric H/O**

**Drug H/O**

- OHA/INSULIN

**General Examination**

- Pallor/Icterus/Cyanosis/Clubbing/Lymphadenopathy/Edema
- Height: cms Weight: kgs BMI

**Vital data**

- Temp | Pulse | RR | BP
- Systemic examination
- P/A-
- Fundus

**Provisional diagnosis**

**Investigations**

| CBP: Hb% | CUE: Pr: | RBC: |
|----------|----------|------|
| 24 hr Urinary prot | /day | Sug: |

| RBS: mg/dl | FBS: mg/dl | PLBS: mg/dl |
|------------|------------|-------------|
| HbA1C:     |            |             |
| Bl. Urea:  | mg/dl      | Sr Creat:   |
|            |            | mg/dl       |
Sr Na+: meq/L  
Sr proteins: Total- G/dl  
Sr Ca++: mg/dl  
K+: meq/L  
Sr albumin: G/dl  
Sr Bilirubin-: mg/dl

CT, BT:
USG abdomen: Rt kidney  
Lt Kidney
Renal biopsy
• LM  
• IF

Diagnosis

Observations
This prospective study was carried out from Dec 2013 to Dec 2015 in Department of Nephrology, Gandhi hospital. Of 139 diabetic patients with renal dysfunction admitted, 77 patients i.e those patients with contracted kidneys (43), acute precipitating event (8) and patients who are unwilling for biopsy(26) were excluded from the study. A total of 62 diabetic patients with renal dysfunction who underwent renal biopsy were studied. Type1 Diabetes was present in 2 cases and 60 cases had type 2 Diabetes.

Of 62 patients studied 45 patients had Diabetic nephropathy and 17 patients had Non diabetic renal disease.

Age Distribution
Average age of study population was 49.96±8.06 years with youngest patient being 30 Yrs of age and eldest being 70 yrs of age.70% of sample are between 41-60 yrs of age.

|AGE IN YEARS| STUDY SAMPLE |
|------------|--------------|
|0-20        | 0            |
|21-40       | 9            |
|41-60       | 49           |
|>60         | 4            |
|TOTAL       | 62           |

Gender Distribution
Of the 62 cases 49 were male and 13 were females with a male:female ratio is 3.7:1

Duration Of Diabetes
In the present study mean duration of diabetes was 6.95 ± 4.36 years in DN cases and 5.69 ± 4.25 years in NDRD cases.
Histopathology
Of 62 cases studied 45(72.5%) cases had Diabetic nephropathy -DN, 17(27.4%) cases had nondiabetic renal disease-NDRD on histopathology.

Pathological Classification of DN

| CLASS    | No of Cases | Percentage |
|----------|-------------|------------|
| Class I  | 2           | 4%         |
| Class IIa| 2           | 4%         |
| Class IIb| 5           | 11%        |
| Class III| 14          | 31%        |
| Class IV | 22          | 49%        |
| TOTAL    | 45          | 100%       |

Histopathological Classification of diabetic renal disease

Of the 45 cases with diabetic nephropathy on histopathology, most common Class of DN was Class IV observed in 22(49%) cases, followed by Class III DN observed in 14(31%) cases, followed by Class IIa(4%) and Class IIb (11%), followed by Class I DN observed in 2(4%) cases

Non Diabetic Renal Disease

| Disease         | No of Cases |
|-----------------|-------------|
| IgA Nephropathy | 4           |
| FSGS            | 3           |
| Membranous N    | 1           |
| C3GN            | 1           |
| PIGN            | 2           |
| HTN Nephropathy | 4           |
| CN              | 1           |
| ATIN            | 1           |
| TOTAL           | 17          |

In the present study glomerular lesion were seen in 15(88.3%) cases and tubulointerstitial lesions were seen in 2 (11.7%) cases. Most common NDRD in present study was IgA Nephropathy seen 4(23.5%) cases. Cresentric GN was observed in 1 case.

Diabetic Retinopathy

Of the 62 cases, 32 pts (51.6%) had diabetic retinopathy and 30 patients (48.3%) did not have diabetic retinopathy.

Of the 32 cases who had diabetic retinopathy 23 cases (71.8%) had DN, 9cases (28.1%) had NDRD. Of 30 cases who did not have diabetic retinopathy 22 cases (73.3%) had DN on biopsy.

|              | DR  | NO DR |
|--------------|-----|-------|
| DN           | 23  | 22    |
| NDRD         | 9   | 8     |
| TOTAL        | 32  | 30    |

Presence or absence of diabetic retinopathy poorly correlated with presence or absence of DN (p value-0.8)
Both cases of Class I DN and Class IIa did not have DR, (20%) of cases of Class IIb DN had DR, (50%) of Class III DN had DR and (68.1%) of cases with Class IV DN had DR.

Presence of diabetic retinopathy correlated with higher class of diabetic nephropathy (p -0.03)

| CLASS   | DR | NO DR |
|---------|----|-------|
| I       | 0  | 2     |
| IIa     | 0  | 2     |
| IIIb    | 1  | 4     |
| III     | 7  | 7     |
| IV      | 16 | 6     |
| TOTAL   | 24 | 21    |

Presence of hypertension didn’t predict the presence or absence of DN (p -0.94)

|           | NORMATENSIVE | HYPERTENSIVE |
|-----------|--------------|--------------|
| CLASS I   | 2            | 0            |
| CLASS IIa | 1            | 1            |
| CLASS IIb | 1            | 4            |
| CLASS III | 2            | 12           |
| CLASS IV  | 5            | 17           |

Presence of Hypertension didn’t correlate with class of Diabetic nephropathy (p value-0.1)

DN Class & Duration of Diabetes
Mean duration of diabetes in cases with diabetic nephropathy was 6.9±4.22 yrs. Mean duration of DN in NDRD was 5.64±4.36yrs.

| CLASS   | 0-5YEARS | 6-10YEARS | >10YEARS |
|---------|----------|-----------|----------|
| DN      | 21       | 19        | 5        |
| NDRD    | 9        | 7         | 1        |
| TOTAL   | 30       | 26        | 6        |

Of 45 cases with DN, 21 (46.6%) cases had DM for <6 yrs and 5(11%) cases had DM for >10 yrs. Of 17 cases of NDRD, 9 (52.9%) cases had DM for <6yrs and 1 (5.8%) case had DM for >10 yrs

Duration of diabetes didn’t predict presence or absence of DN (p value-0.79)

| CLASS OF DN | 0-5YEARS | 6-10YEARS | >10YEARS |
|-------------|----------|-----------|----------|
| CLASS I     | 2        | 0         | 0        |
| CLASS IIa   | 1        | 1         | 0        |
| CLASS IIb   | 2        | 3         | 0        |
| CLASS III   | 4        | 9         | 1        |
| CLASS IV    | 10       | 8         | 4        |
| TOTAL       | 19       | 21        | 5        |

DN & Hypertension
Of the 62 cases of diabetic patients with renal dysfunction 46 (74.1%) cases had hypertension. 34 (75%) hypertensive cases had diabetic nephropathy and 12 (70.5%) cases have NDRD.
Duration of diabetes didn't correlate with class of DN (p value-0.53)

Hematuria and Renal histology
Of the 62 cases, 6 cases had microscopic hematuria. of these cases 3 had Ig A Nephropathy 2 had PIGN 1 had C3GN nephropathy. Due to small number of cases statistical analysis could not be made.

DN Vs Proteinuria
Mean 24 hr urinary protein in patients with DN was 1.98±1.85 g/day and mean 24hr urinary protein in NDRD was 1.8±1.89g/day

Degree of proteinuria didn’t differentiate DN from NDRD (p value-0.17)
Of 17 NDRD cases, 10(58%) had subnephrotic range proteinuria and 7(41.1%)had nephrotic range proteinuria.80% DN cases had nephrotic range proteinuria and 20% had subnephrotic range proteinuria.

Higher Degree of proteinuria is associated with advanced class of DN(p value-0.03)
DN Vs Glycemic control during admission

13(28.8%) of 45 patients with DN had good glycemic control vs 6(35.2%) of 17 patients with NDRD at the time of admission.

|                         | Good Glycemic Control | Poor Glycemic Control |
|-------------------------|-----------------------|-----------------------|
| DN                      | 13                    | 32                    |
| NDRD                    | 6                     | 11                    |
| TOTAL                   | 19                    | 43                    |

Blood sugars at the time of admission poorly correlated with DN with p value-0.75

Glycemic control poorly correlated with the class of Diabetic nephropathy(p value-0.18)

DN vs. eGFR

Mean eGFR in DN was 19.69 ± 11.69 ml/min/1.732m² and mean eGFR of cases with NDRD was 18.4 ± 11.98 ml/min/1.732m².

|                          | Good Glycemic Control | Poor Glycemic Control |
|--------------------------|-----------------------|-----------------------|
| CLASS I                  | 0                     | 2                     |
| CLASS IIA                | 0                     | 2                     |
| CLASS IIB                | 2                     | 3                     |
| CLASS III                | 7                     | 7                     |
| CLASS IV                 | 4                     | 18                    |
| TOTAL                    | 13                    | 32                    |

Of 62 diabetic cases 2(3%) cases have eGFR>60 ml/min/1.732m² and 27 (43.5%) cases with eGFR<15 ml/min/1.732m² required renal replacement therapy either in the form of hemodialysis or peritoneal dialysis.

eGFR poorly correlated with DN (p value0.75)

Correlation of baseline eGFR and histology:

Mean eGFR of cases at after stabilisation of patients (baseline GFR) in DN Class I, IIA, IIB, III

|                          | >90  | 89-60 | 59-30 | 29-15 | <15  |
|--------------------------|------|-------|-------|-------|------|
| DN/NDRD                  |      |       |       |       |      |
| DN                       | 0    | 1     | 5     | 21    | 18   |
| NDRD                     | 0    | 1     | 2     | 5     | 9    |
| TOTAL                    | 0    | 2     | 7     | 26    | 27   |

Higher class of DN is associated with lower eGFR i.e 50% of CLASS III and 50% of CLASS IV have eGFR<15 ml/min/1.732m² respectively

|                          | >90  | 89-60 | 59-30 | 29-15 | <15  |
|--------------------------|------|-------|-------|-------|------|
| CLASS I                  | 0    | 0     | 0     | 2     | 0    |
| CLASS IIA                | 0    | 1     | 0     | 1     | 0    |
| CLASS IIB                | 0    | 0     | 1     | 4     | 0    |
| CLASS III                | 0    | 0     | 1     | 6     | 7    |
| CLASS IV                 | 0    | 0     | 2     | 9     | 11   |
| TOTAL                    | 0    | 1     | 4     | 22    | 18   |

Lower the eGFR higher the DN Class. (p value<0.02)
Discussion
The progressive increasing incidence of diabetic nephropathy in present population has significant implication on social and economic resources of the developing nations. Furthermore, prognosis in such patients is very poor compared with patients with ESRD due to other renal diseases. Proteinuria in diabetic patients is usually interpreted as a clinical manifestation of diabetic nephropathy. Although kidney biopsy is the most unbiased method of evaluation it is rarely used in these subjects. The primary aim of kidney biopsy in proteinuric patients with diabetic nephropathy is to confirm/exclude non-diabetic renal disease.

In 2010 Research Committee of the Renal Pathology Society (RPS) developed a consensus classification combining type 1 and type 2 diabetic nephropathies by Tervaert et al in this classification, diabetic nephropathy is divided in to four hierarchical glomerular lesions with separate evaluation for interstitial and vascular lesions. However the clinical utility of this pathological classification for predicting outcomes is not established.

This study aimed to evaluate the relationship between histological changes and clinical parameters in diabetic patients with renal dysfunction. There are no standardized criteria for renal biopsy in DN, therefore obtaining a renal biopsy from patients with DN is currently a matter of judgment by the Nephrologist. Currently, renal biopsy is commonly performed in patients who show the following features:

- Renal manifestations are seen atypically (<10 years) early in type 1 diabetes
- Dysmorphic erythrocytes/casts are found in urine (nephritic sediment)
- Rapid deterioration of renal function of unknown cause is noted
- Elevated serum creatinine without urine abnormalities
- Macroalbuminuria without retinopathy

Heavy proteinuria (>8 g/day).

Biopsy not indicated when
- Typical evolution of renal disease
- Concomitant retinopathy is present.

Although pathologic classifications exist for several renal diseases, a uniform classification for diabetic nephropathy is lacking. In 2010 Research Committee of the Renal Pathology Society (RPS) developed a consensus classification combining type 1 and type 2 diabetic nephropathies. The reported incidence of NDRD ranged from 23-54% in proteinuric type 2 DM patients. Non-diabetic renal diseases often develop in diabetic patients with proteinuria. Therefore, kidney biopsy may become a useful diagnostic option among proteinuric patients with this type of diabetes mellitus.

With this background we analysed 62 cases of diabetes mellitus presenting with renal dysfunction (proteinuria or high serum creatinine) who underwent renal biopsy with or without classical indications of renal biopsy in diabetes and classified cases according to The Renal Pathology Society classification. In the present study of type I and Type II diabetic cases are classified together as suggested in renal pathology society classification and clinicopathological correlation was analysed.

Of the 62 cases 49 were male and 13 were females with a male to female ratio of 3.7: 1, slightly higher in comparison to studies by J Prakash et al of 1.87: 1 and 2:1 in study by Koji Harada et al. Mean age of cases in present study was 49.96±8.06 years, similar to observations made by 50.68±11.29yrs in study by Amal Abdel Ghani et al. In the present study mean duration of diabetes was 6.9±4.22yrs. Mean duration of diabetes was 9 ± 6.8 yrs in study by Sonia yaqub, 9.33± 3.6yrs in study by Amal Abdel Ghani etal and 10.1 ± 8.5 years in study by Koji Harada etal.

In the present study non diabetic renal disease (NDRD) on histopathology was present in 17(27.4%) of cases on par with Parving et al study which also showed that eight (23%) of 35 type 2 diabetic patients had NDRD. Gambara et al.
reported that 17 (32.7%) of 52 type 2 diabetic patients had NDRD. A study done by J prakash et al showed an incidence of NDRD in 7(30.4%) of 23 cases of type 2 DM. Variation in incidence could due to selection bias for indication of biopsy. A meta analysis of data available on prevalence of non-diabetic kidney disease among type 2 diabetic patients done by Zukowska-Szczechowska E et al, revealed that NDRD was evident on kidney biopsy approximately in 22% of European and 26.7% of Asian patients with type 2 diabetes mellitus similar to the present study and was observed that even after adjusting for differences in methodology among the studies, NDRD may affect a significant percentage of patients with type 2 diabetes mellitus. Therefore, kidney biopsy may become a useful diagnostic option among proteinuric patients of diabetes mellitus.

In the present study glomerular lesions were seen in 15(88.2%) cases and tubulointerstitial lesions were seen in 2 (11.7%) cases. Most common NDRD in present study was IgA nephropathy seen in 4(13.5%) cases. Most common glomerular diseases were Ig A Nephropathy, Crescentic GN observed in 1 (5.8 %) cases each at par with the meta analysis by Zukowska-Szczechowska E et al, in which IgA nephropathy was consistently the most common type of glomerulonephritis in both Caucasian and nonCaucasian populations accounting for approximately 6-19% of kidney biopsies. In the study by Jianhui Zhou et al also Ig A nephropathy was predominant glomerular lesion accounting for 34% of cases.

In the present study mean duration of diabetes in the study population was 6.95 ± 4.36 yrs, mean duration of diabetes in cases with biopsy proven diabetic nephropathy was 5.69±4.25 yrs. Difference in duration of diabetes in DN and NDRD was not statistically significant with p value-0.79. Similar observations of no statistically significant difference in duration of DM between DN and NDRD (p>0.05)-were found in the studies by U. Das et al, Parving HH et al and study by Amal Abdel Ghani et al. In a study by S. Michael Mauer et al, research renal biopsies were performed in patients who had Type 1 DM for 2.5-29 yr who were selected using no other criteria there was no strong relationship between either glomerular basement membrane (GBM) thickness or mesangial expansion and duration of Type 1 DM. In the present study mean duration of DM in DN Class I, II a, II b, III and IV was 4±2.3,5±4.5. 4.6±3.6, 7.7±3.9 and 7.4 ± 4.2 yrs respectively. There was no statistically significant difference in duration of diabetes and class of DN with p-0.523. Melvin M. Schwartz et al noted that there was significant difference in duration of diabetes between patients with K-W lesions and mesangial lesions.

Of the 62 cases, 32 pts (51.6%) had diabetic retinopathy, of which 23 cases (71.8%) had DN, 9 cases (28.1%) had NDRD. In study of renal biopsy in patients with presumed diabetic nephropathy by Koji Harada et al of the 21 cases with DR 18 (85.7%) had DN, J Prakash reported 9(60%) cases with retinopathy had DN and 40% had NDRD. Of 30 cases who did not have diabetic retinopathy 22 cases (73.3%) had biopsy proven DN on par with a study done by Perk. Christensen et al of 52 patients with type 2 diabetes without diabetic retinopathy, 35(69%) patients had diabetic nephropathy on biopsy, Serra et al reported that diabetic glomerulosclerosis was diagnosed in 17(74%) of patients without diabetic retinopathy. Schwartz MM et al noted 7 0f 8(87.5%) patients without retionopathy had mesangiosclerosis characteristic of DN, J prakash et al noted that 4 of 8 (50%) cases without DR had DN. It should be pointed out that absence of retinopathy cannot exclude the presence of diabetic nephropathy. Clearly diabetic nephropathy can occur in absence of retinopathy in Type 2 proteinuric diabetic patients.

Type 2 diabetic patients with typical diabetic nephropathy on biopsy did not have diabetic retinopathy in the study by J prakash et al, Parving et al noted that 40% of proteinuric Type
2 DM patients lacked diabetic retinopathy. Of 20 cases of NDRD 8 (40%) cases had diabetic retinopathy, in study by Prakash J et al. 

Management of cases with NDRD grossly differs from that of DN, if biopsy is not done in patients with DR presuming diagnosis of DN significant number of NDRD requiring specific therapy might be missed.

**Presence or absence of Diabetic retinopathy poorly correlated with presence or absence of diabetic nephropathy p value -0.8**

Thus renal biopsy is necessary for precise diagnosis of diabetic and non-diabetic renal lesions in proteinuric Type 2 diabetic patients even in the presence of diabetic retinopathy.

In the present study both cases of Class I DN, Class IIa did not have DR, 20% of cases of Class IIb DN had DR, 50% of Class III DN had DR and 68.8% of cases with Class IV DN had DR.

**Presence of diabetic retinopathy correlated with higher class of diabetic nephropathy (p value-0.03)**, similar observations were noted by Koji Harada et al15 patients with both DN and DR showed more severe renal histology than those without DR. Melvin M. Schwatz et al noted that patient with K-W lesions had correlation with retinopathy but not mesangial sclerosis, similar observations were made in type 1 DM also by Blanchem. Chavers et al.16

Mean 24 hr urinary protein in patients with DN was 1.98±1.85 g/day and mean 24hr urinary protein in NDRD was 1.8±1.89 g/day. **Degree of proteinuria didn’t differentiate DN from NDRD (p value-0.17)**

Mean 24hr urinary protein in DN Class I, IIa, IIb, III and IV was 0.68±0.96, 0.7±2.06,1.66 ±1.84, 2.2±1.85 and 2.14+1.85 g/day respectively. **Degree of proteinuria correlated with class of DN (p-value-0.03)**, similar observations were made by Kathryn Elizabeth White, RuthoSterby etal where severity of proteinuria correlated with index of structural lesions.

13 (28%) of 45 cases of DN had poor glycemic control. 6 (35%) of 17 cases of NDRD had poor glycemic control. **Glycemic control at time of biopsy could not predict DN or NDRD p value -0.75.** Similar observations were made by parving et al.4 with a p value >0.5.

**Glycemic control poorly correlated with class of diabetic nephropathy p value -0.18.** Melvin M. Schwartz et al13 noted that glycemic control correlated poorly with patients with KW lesions and mesangial sclerosis.

Of the 45 cases with DN, 34 (75.5%) cases had hypertension. and 11(24.4%) cases have normotension. Of 17 cases with NDRD 12(70.5%) were hypertensive.

**Hypertension did not differentiate between DN and NDRD (p value-0.94).** similar observations were made by Amal Abdel Ghani etal5, Vincenzo Gambara etal10, Sonia yaqub etal17.

77.2% of cases with Class IV DN had HTN. **Presence of hypertension did not correlate with class of Diabetic nephropathy (p value-0.1)**

Mean eGFR in DN was 19.69 ± 11.69 ml/min/1.732m² and mean eGFR of cases with NDRD was 18.4 ± 11.98 ml/min/1.732m². Higher class of DN is associated with lower eGFR i.e 50% of CLASS III and 50% of CLASS IV have eGFR<15 ml/min/1. 732m² **mean eGFR didn’t differentiate between DN and NDRD (p value-0.75)**

Mean eGFR of cases at after stabilisation of patients (baseline GFR) in DN Class I, IIa, IIb, III and IV was 24±7.7, 45.5±12.9,25. 6±12.6, 17.6±13.1, 17.01±11.69 ml/min/1.732m² respectively, with a significant difference between DN classes p value<0.020. **Lower the eGFR higher the DN Class (p value-0.02).** Melvin M. Schwartz et al noted that there was significant difference in creatinine clearance between patients with K-W lesions and mesangial lesions.

**Conclusions**

1) Non diabetic renal disease constitutes significant percentage of patients with clinical diabetic nephropathy patients and its presence is highly underestimated.
2) Ig A is most common histopathological lesions among NDRD patients.
3) The most common histopathological lesion was diabetic nephropathy among all diabetic patients with renal dysfunction.
4) Majority of patients with diabetic nephropathy are CLASS IV.
5) Higher degree of proteinuria, presence of diabetic retinopathy, low eGFR hypertension correlated with higher classes of diabetic nephropathy.
6) Degree of proteinuria, duration of diabetes, diabetic retinopathy and glycemic control, poorly predicted the occurrence of NDRD.
7) Renal biopsy is the unbiased method for precise diagnosis of diabetic and non diabetic renal lesions.

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Abbreviations
DM - Diabetes Mellitis
HTN - Hypertension
PDR- Proliferative Diabetic Retinopathy
NPDR- Non Proliferative Diabetic Retinopathy
CSME- Clinically Significant Macular Edema
HEP B-Hepatitis B
HEP C-Hepatitis C
PN-Peripheral Neuropathy
CVA-Cerebro Vascular Accident
CAD-Coronary Artery Disease
eGFR-Estimated Glomerular Filtration Ratio
DN-Diabetic Nephropathy
NDRD-Non Diabetic Renal Disease
C3GN-C3 Glomerulonephritis
ATIN-Acute Tubulointerstitial Nephropathy
CIN-Chronic Interstitial Nephritis
PIGN-POST Infectious Glomerulonephritis