JMSCR Vol||05||Issue||11||Page 30002-30014||November 2017

www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 71.58
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i11.32

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

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 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 comparsion 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 type1 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.

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 immunoflourescence 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, CIq, and Fibrinogen. The intensity was semiquantatively 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 odema/ SOB/
- H/o Azotemia
- H/o blurring of vision/retinal surgeries/laser photocoagulation
- H/o parasthesias
- H/o recent GE/ precipitaing factors
- H/o usage of nephrotoxic drugs/herbal medicine intake

Past History

– HTN/CKD/CAD/TB/asthma/epilepsy

Family History

-DM/HTN/CKD/

Menstrual & Obstretic 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 K +: meq/L

Sr proteins: Total- G/dl Sr albumin : G/dl

Sr Ca++ : mg/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.

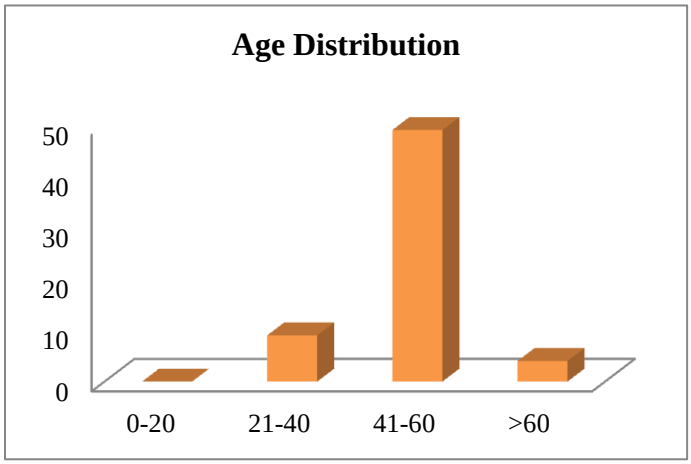
Of 62 patients studied 45 patients had Diabetic nephropathy and 17 patients had Non diabetic renal disease.

Age Distribution

Average age of study population was 49.96±8.06 years with youngest patient being 30

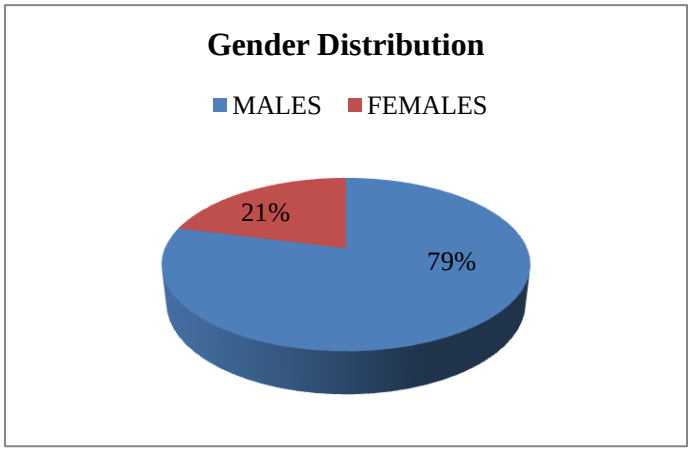
Yrs of age and eldest being 70 yrs of age.70% of sample are between 41-60 yrs of age.

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



Gender Distribution

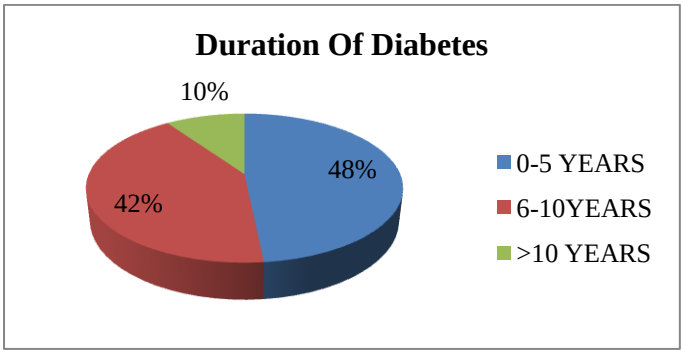
Of the 62 cases 49 were male and 13 were females with a male:female ratio is 3.7:1



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.

Duration In Years	No Of Cases	Percentage
0-5 Years	30	48%
6-10years	26	42%
>10 Years	6	10%
Total	62	100%



Histopathology

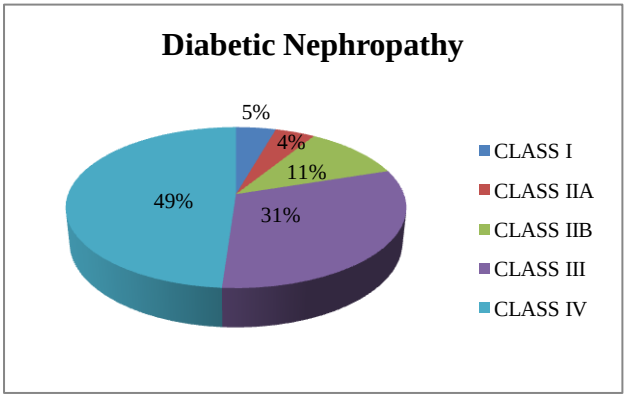
Of 62 cases studied **45(72.5%) cases had Diabetic nephropathy -DN**, **17(27.4%) cases had nondiabetic renal disease-NDRD** on histopathology.

Pathological Classification of DN

CLASS I	2	4%
CLASS IIa	2	4%
CLASS IIb	5	11%
CLASS III	14	31%
CLASS IV	22	49%
TOTAL	45	100%

Histopathogical 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

IgA Nephropathy	4
FSGS	3
Membranous N	1
C3GN	1
PIGN	2
HTN Nephropathy	4
CIN	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.

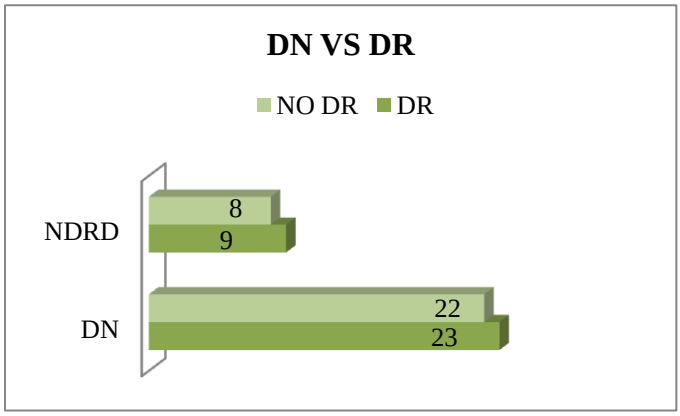
Diabetic Retinopathy

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

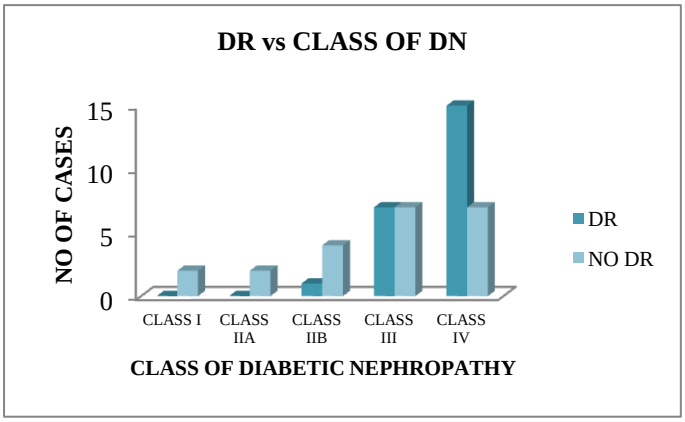
Presence or absence of diabetic retinopathy poorly correlated with presence or absence of DN (p value-0.8)



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.

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

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



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

NO.OF CASES	HTN	Normotension
DN	34	11
NDRD	12	5
TOTAL	46	16

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

	NORMOTENSIVE	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.

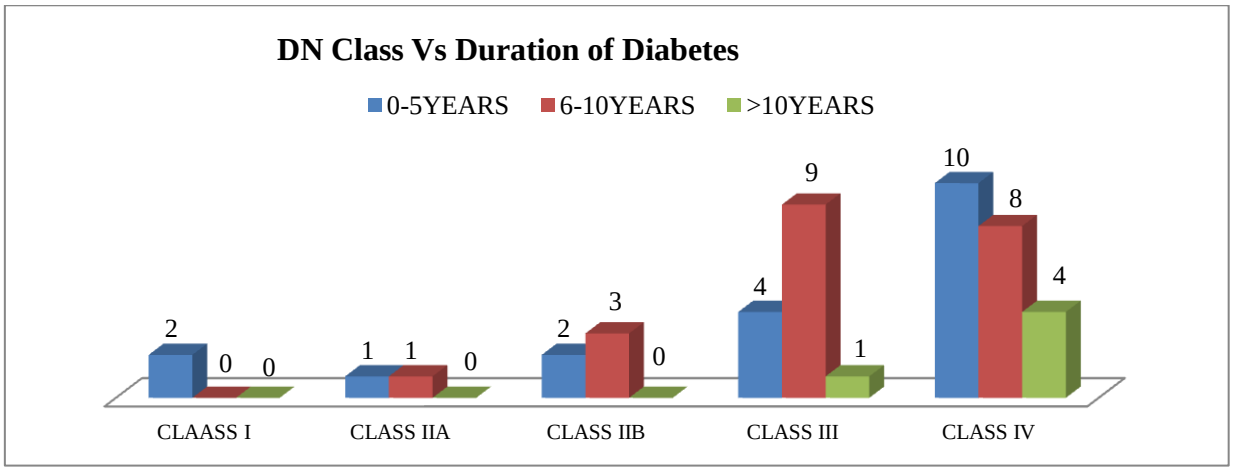
	0-5YEARS	6-10YEARS	>10YEARS
DN	21	19	5
NDRD	9	7	1
TOTAL	30	26	6

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

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 Protienuria

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

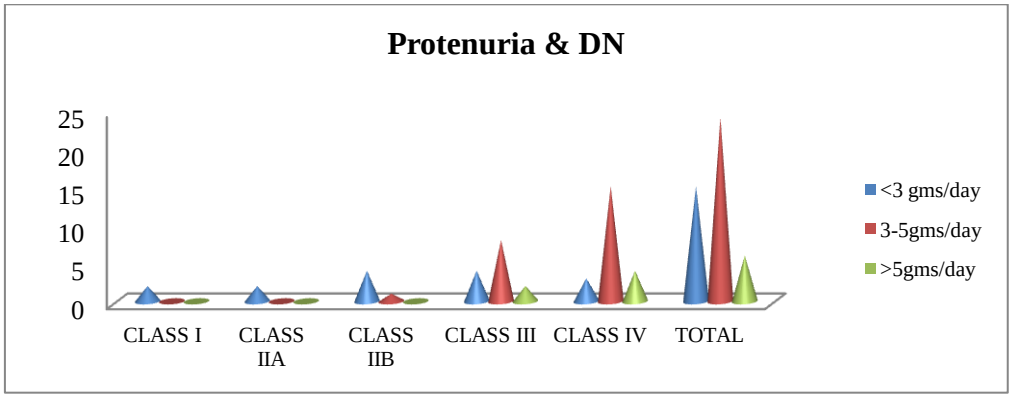
	<3 gms/day	3-5gms/day	>5gms/day
DN	15	24	6
NDRD	10	5	2
TOTAL	25	29	8

Degree of protenuria didn't differentiate DN from NDRD (p value-0.17)

Of 17 NDRD cases, 10(58%) had subnephrotic range protenuria and 7(41.1%)had nephrotic range protenuria.80% DN cases had nephrotic range protenuria and 20% had subnephrotic range protenuria.

	<3 gms/day	3-5gms/day	>5gms/day
CLASS I	2	0	0
CLASS IIA	2	0	0
CLASS IIB	4	1	0
CLASS III	4	8	2
CLASS IV	3	15	4
TOTAL	*15*	*24*	*6*

Higher Degree of proteinuria is associated withadvanced 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

	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

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/1.732m^2 and mean eGFR of cases with NDRD was 18.4 ± 11.98 ml/min/1.*732m*^{2}

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

Of 62 diabetic cases 2(3%) cases have eGFR>60 ml/min/1.732m^2 and 27 (43.5%) cases with eGFR<15 ml/min/1.732m^2 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 and IV was 24±7.7, 45.5±12.9,25.6±12.6, 17.6±13.1, 17.01±11.69 ml/min/1.732m^2 respectively

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. 732m^2

	>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 type1 and type 2 diabetic nephropathies by Tervaert et al in this classification, diabetic nephropathy is divided in to four hierarchial 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 with DN who show the following features-

Biopsy should be considered when[6]

- 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
- Macroalbuminura 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 type1 and type 2 diabetic nephropathies[3]

The reported incidence of NDRD ranged from 23-54% in proteinuric type 2 DM patients.[6] 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[3]

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 comparsion to studies by J Prakash etal[5] of 1.87: 1 and 2:1 in study by Koji Harada etal.[7]

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 etal[8]

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[17], 9.33± 3.6yrs in study by Amal Abdel Ghani etal[4] and 10.1 ± 8.5 years in study by Koji Harada etal[67.]

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[4]study which also showed that eight (23%) of 35 type 2 diabetic patients had NDRD. Gambara et al [10]

reported that 17 (32.7%) of 52 type 2 diabetic patients had NDRD. A study done by J prakash etal[1]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 etal[3], 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, Cresentric GN observed in 1 (5.8 %) cases each at par with the meta analysis by Zukowska-Szczechowska E etal[3], 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 etal[11] 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 etal[12], Parving HH etal[4] and study by Amal Abdel Ghani etal[8]. In a study by S. Michael Mauer etal[20], 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. Schwatrz etal[13] 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, 9cases (28.1%) had NDRD. In study of renal biopsy in patients with presumed diabetic nephropathy by Koji Harada etal [7] of the 21 cases with DR 18 (85.7%) had DN, J Prakash[5] 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 etal of 52 patients with type 2 diabetes without diabetic retinopathy, 35(69%) patients had diabetic nephropathy on biopsy, Serra et al[14] reported that diabetic glomerulosclerosis was diagnosed in 17(74%) of patients without diabetic retinopathy. Schwartz MM etal[13] noted 7 0f 8(87.5%) patients without retionopathy had mesangiosclerosis characteristic of DN, J prakash etal [5] 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.(p value-0.8)

Type 2 diabetic patients with typical diabetic nephropathy on biopsy did not have diabetic retinopathy in the study by J prakash etal [5], Parving et al[4]. 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 etal.[75]

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.

Prescence of diabetic retinopathy correlated with higher class of diabetic nephropathy (pvalue-0.03), similar observations were noted by Koji Harada etal[15] patients with both DN and DR showed more severe renal histology than those without DR. Melvin M. Schwatrz etal[13] 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 etal.[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±1.89g/day. ***Degree of protenuria 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 protenuria correlated with class of DN (p-value-0.03)***, similar observations were made by Kathryn Elizabeth White[18], RuthoSterbyetal[19] 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 etal.[4] with a p value >0.5.

Glycemic control poorly correlated with class of diabetic nephropathy p value -0.18.Melvin M. Schwatrz etal[13] 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 etal[5], Vincenzo Gambara etal[10], Sonia yaqub etal[17].

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/1.732m^2 and mean eGFR of cases with NDRD was 18.4 ± 11.98 ml/min/1.*732m^2***.** 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. 732m^2

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/1.732m^2 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. Schwatrz 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.

References

1. Kramer CK, Leitao CB, Pinto LC, Silveiro SP, Gross JL, Canani LH: Clinical and laboratory profile of patients with type 2 diabetes with low glomerular filtration rate and normoalbuminuria. *Diabetes Care* 2007, 30:1998-2000.
2. Fioretto P, Steffes MW, Sutherland DE, Goetz FC, Mauer M: Reversal of lesions of diabetic nephropathy after pancreas transplantation. *N Engl J Med* 1998, 339:69-75.
3. Zukowska-Szczechowska E, Tomaszewski M. Renal affection in patients with diabetes mellitus is not always caused by diabetic nephropathy. Annales Academiae medicae Bialostocensis 2004;49:185-189
4. Parving HH, Gall MA, Skott P, Jorgensen HE, et al. Prevalence and causes of albuminuria in non-insulin-dependent diabetic patients. Kidney Int 1992;41:758–62.
5. J Prakash, M Lodha, SK Singh, et al.Diabetic Retinopathy is A Poor Predictor of Type of Nephropathy in Proteinuric Type 2 Diabetic Patients. JAPI JUNE 2007; 55 :412-416
6. Jai prakash Non-Diabetic Renal Disease (NDRD) in Patients with Type 2 Diabetes Mellitus (Type 2 DM). JAPI 2013; 61:194-199
7. Koji Harada etal.. Significance of renal biopsy in patients with presumed diabetic nephropathy. Journal of Diabetes Investigation 2013; 4 (1), p88-93.
8. Amal Abdel Ghani etal.. Renal biopsy in patients with type 2 diabetes mellitus: indic ations and nature of lesions. Ann Saudi Med 2009;29(6):450-453.
9. S. Michael Mauer, Michael W. Steffes etal.. Structural-Functional Relationships in Diabetic Nephropathy. J. Clin. Invest. 1984; 74: 1143-1155.
10. Gambara V, Mecca G, Remuzzi G, Bertani T. Heterogeneous nature of renal lesions in type II diabetes. J Am Soc Nephrol 1993;3: 1458-1466.
11. Jianhui Zhou etal..A differential diagnostic model of diabetic nephropathy and non-diabetic renal diseases. Nephrol Dial Transplant 2008; 23: 1940–1945.
12. U.Das, Dakshinamurthy, etal..Non diabetic renal disease in type 2 diabetic patients: Single centre experience. Indian Journal of nephrology 2012;22(5): 358-362
13. Schwartz MM etal. Renal pathology patterns in type II diabetes mellitus: relationship with retinopathy. Nephrol Dial Trasnsplant 1998;13:2547-2552.
14. Serra A, Romero R, Bayes B et al. Is there a need for changes in renal biopsy criteria in proteinuria in Type 2 diabetes? Diabetes Research and Clinical Practice 2002;58:149-53.
15. Prakash J etal.. Non-Diabetic Renal Disease in Patients with Type 2 Diabetes Mellitus J Assoc Physicians India. 2001;49:415-20.
16. Blanchem. Chavers, S. Michaelmauer etal. Relationship between retinal and Glomerular lesions in IDDM patients. DIABETES 1994;43:p 441-446.

17. Sonia yaqub etal..Non-Diabetic renal disease in in patients with type 2 diabetes mellitus. Saudi J Kidney Dis Tanspl 2012;23(5): 1000-1007.
18. . Kathryn Elizabeth White and Rudolf William Bilous etal.. Type 2 Diabetic Patients with Nephropathy Show Structural– Functional Relationships that Are Similar to Type 1 Disease. J Am Soc Nephrol 2000;11: 1667–1673.
19. Ruth Osterby, Hans-Henrikparving, Glomerular Structure and Function in Diabetic Nephropathy Early to Advanced Stages. DIABETES, 1990; 39:1057-1063

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 Tubulointerstial Nephropathy
CIN-Chronic Interstitial Nephritis
PIGN-POST Infectious Glomerulonephritis