RENAL FUNCTION IN NON-INSULIN DEPENDENT DIABETES MELLITUS-A FOLLOW-UP STUDY

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Summary :

Assessment of renal function was done in one hundred non-insulin dependent diabetes mellitus patients with varying duration of diabetes, attending the Diabetes Research Centre, Madras. The parameters studied included blood urea, serum creatinine, creatinine clearance and 24 hour urinary protein excretion.

The patients were followed up and the renal function tests were repeated at periodical intervals. Diabetic nephropathy was diagnosed if urinary protein excretion (UPE) was more than 500 mg/day; those with UPE of 150-499 mg/day were considered having raised proteinuria (RP) and those with a creatinine clearance of more than 150 ml/mt were considered as having hyperfiltration.

Analysis of the results of follow-up showed :

1. The incidence of diabetic nephropathy peaked at 11-15 years of diabetes.
2. 42% of patients with RP developed diabetic nephropathy
3. 25% with hyperfiltration developed diabetic nephropathy even though they did not have abnormal UPE initially.

Introduction :

As per the National Diabetic Data Group (NDDG) statistics (1986), it is said that after 15 years of diabetes 1/3 of IDDM and 1/5 of NIDDM develop clinical diabetic nephropathy which is defined as more than 500 mg UPE/day[1,2] This is detectable by the heat test. The development of diabetic nephropathy follows a predictable pattern in IDDM which is well studied and ample literature is available regarding this [3,4,5]. Even though NIDDM comprises of 80-90% of the diabetic population, the course of clinical nephropathy in NIDDM is not very clear due to various reasons like lack of follow-up studies, delayed detection of diabetes mellitus itself, high incidence of associated risk factors influencing kidney damage like hypertension, ischaemic heart disease with congestive cardiac failure, urinary tract infection and the natural regression of glomerular filtration rate due to aging etc. Hence with the aim of understanding the natural history of diabetic nephropathy 100 NIDDM patients of varying duration of disease with follow-up were studied.

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Material and Methods :

100 patients attending the Diabetes Research Centre, Madras, were selected at random in whom complete renal function tests were done in follow-up for atleast 2-3 times. The duration of diabetes varied from 0-25 years at the first visit to our Centre. And the follow-up of these patients was for 5 years on average (4 months - 18 years). These patients are divided into 5 groups according to the duration of diabetes mellitus at the first visit. Group I=0-5 years, Group II = 6-10 years, Group III = 11-15 years, Group IV = 16-20 years, Group V = more than 20 years. In addition to the evaluation of blood sugar status in each visit, RFT was assessed periodically. It consisted of blood urea, creatinine and 24 hour urinary protein estimation and creatinine clearance. The presence of associated complications like ischaemic heart disease, hypertension, peripheral neuropathy and retinopathy were also recorded.

Proteinuria and GFR analysis :

The urinary protein excretion upto 150 mg/day was considered as normal, while urinary protein excretion of more than 500 mg/day was taken as clinical diabetic nephropathy. Hence the urinary protein excretion of 150-499 mg/day was considered as raised proteinuria (RP).

Glomerular filtration rate assessment was made by creatinine clearance estimation. When the normal range was 80-130 ml/min, patients with more than 150 ml/min were considered to have hyperfiltration[6,7].

Proteinuria during the first visit in each group of patients and at follow-up was tabulated. Similarly creatinine clearance at the first visit and at follow-up was also noted in each group.

Patients with raised proteinuria were studied particularly to look at the progression of proteinuria (Fig. - 2) The follow-up of raised proteinuria was done as three groups:

RP → Normal (RP→N)

RP → Persisting in the same range (RP → Persisting)

RP → Progression to diabetic nephropathy (RP → DNY)

Results :

The results are shown in Fig. - 1 and Table - l. Fig. - 1 reflects the picture of renal status of each group at the first visit. This shows that the incidence of clinical diabetic nephropathy peaks when the duration of diabetes mellitus is 11-15 years.

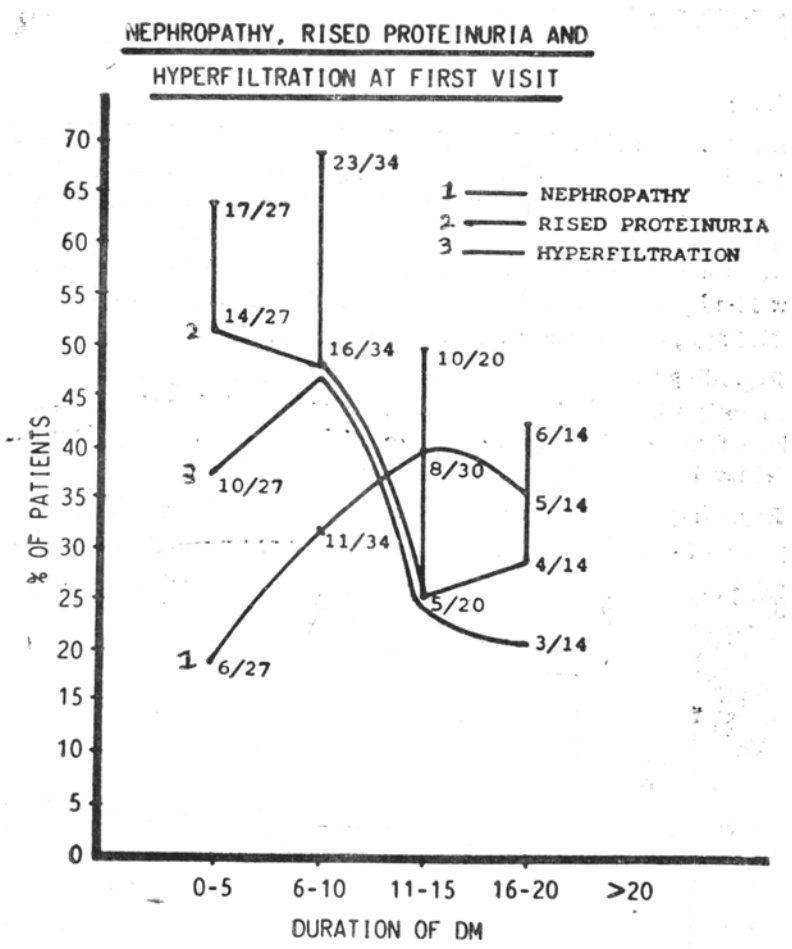

Fig. 1 Renal function in NIDDM—a follow up study

Table I

Renal Status of 100 Patients at First Visit

Status	27 Gr. I 0-5 Yr.	34 Gr. II 6-10 Yr.	20 Gr. III 11-15 Yr.	14 Gr. IV 16-20 Yr.
% Nephropathy	19	32	40	36
% Raised Proteinuria	52	47	25	26
% Hyperfiltration	37	47	25	21

Whereas the incidence of raised proteinuria peaks earlier, at 6-10 years.

Discussion :

It is seen that the raised proteinuria when seen in the initial 5 years of diabetes mellitus gets normalised dramatically during the follow-up (nearly 65%). Whereas, when raised proteinuria is seen in later years with longer duration of diabetes mellitus, many progress to diabetic nephropathy as expected[8,9] (Fig. -2). And here also the progression of raised proteinuria to diabetic nephropathy peaks at 11-15 years of duration of diabetes mellitus. The over all picture is that 30% →N, 28% persisting as RP and 42% →DNY.

Regarding hyperfiltration, it is seen that 29% of our patients had hyperfillration, mostly when the duration of diabetes mellitus is less than 10 years. And in the later follow-up 25% progressed to diabetic nephropathy irrespective of the initial level of urinary protein excretion.

Regarding the other associated complications, ischaemic heart disease, hypertension, peripheral neuropathy and diabetic retinopathy were all on the rise as the duration of

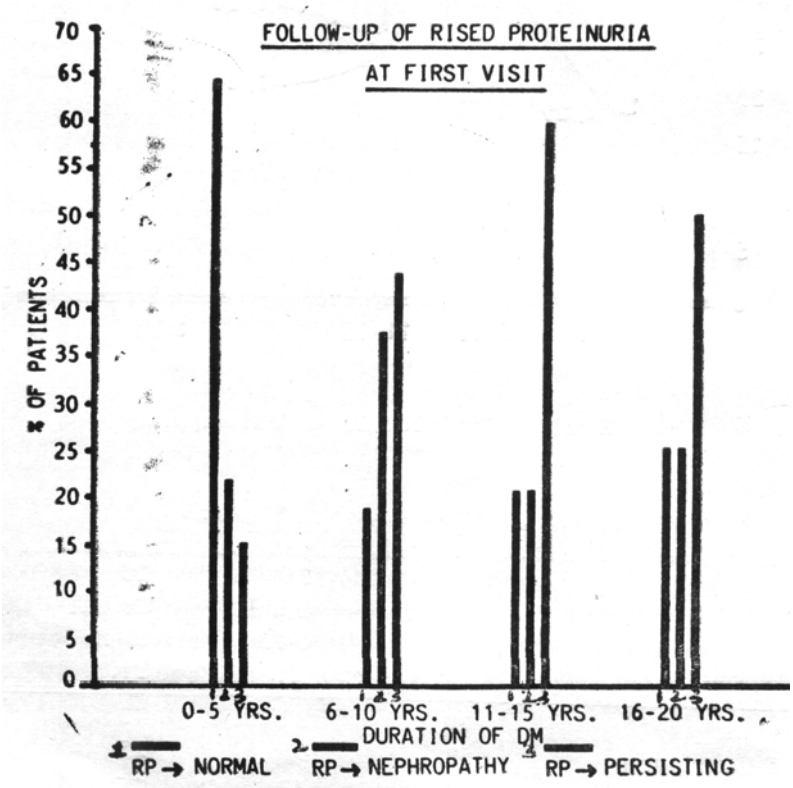

Fig. 2 Renal function in NIDDM—a follow up study

diabetes mellitus increased[10]. But the rise was very much higher for hypertension and retinopathy, both at first visit and at our follow-up which is also tabulated. Retinopathy is higher than nephropathy in our series. For comparison the peak incidence for diabetic nephropathy was 40% in Group III while retinopathy was 50 and 57% in Group III and IV patients respectively at the first visit itself (Fig. 3; Table-2).

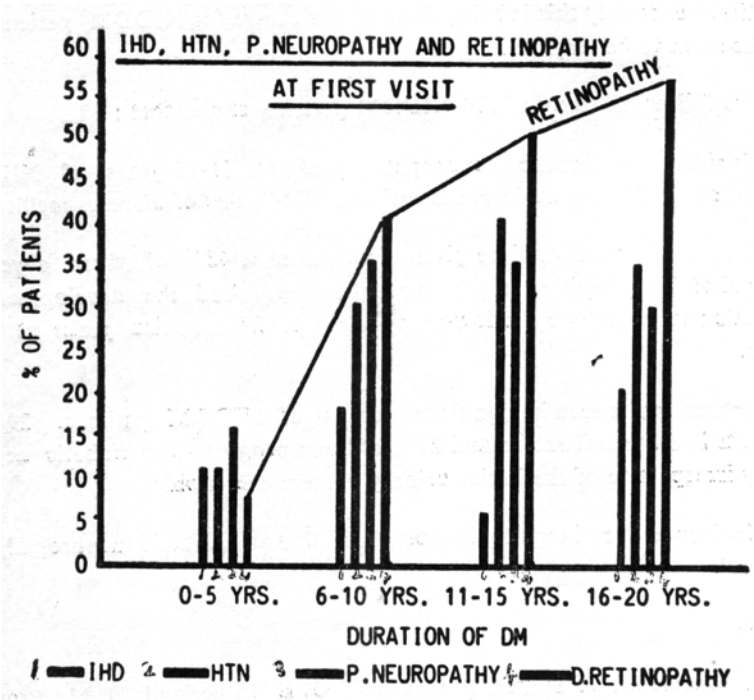

Fig. 3 Renal function in NIDDM—a follow up study

Table 2

Ischaemic heart disease, Hypertension, Peripheral Neuropathy and Retinopathy at Ist Visit and at Follow-up

No.	Complications	Group I 0-5 Yrs.	Group II 6-10 Yrs.	Group III 11-15 Yrs.	Group IV 16-20 Yrs.
1.	% Ischaemic heart disease	11→26	18→38	5→40	21→50
2.	% Hypertension	11→37	26→53	40→70	36→71
3.	% Peripheral neuropathy	15→22	35→44	35→50	29→43
4.	% Diabetic Retinopathy	7→33	38→71	50→80	57→71

Institution of renal function test at the very early stage of diabetes is important and regular follow-up of these individuals may play a great part in the prevention of nephropathy[11,12].

Now detection of microalbuminuria is done which estimates the albumin fraction of urinary protein separately. This predicts nephropathy at the earliest in diabetics. Presently this is being done at our centre for NIDDM patients and the results seem to be very exciting[13].

This follow-up study of 100 NIDDM patients shows that :

1. The incidence of diabetic nephropathy peaks at 11-15 years of NIDDM, whereas raised proteinuria peaks earlier at 0-10 years of diabetes mellitus.

2. Raised proteinuria should be given significance as 42% of them developed clinical diabetic nephropathy in our follow-up. And the development of diabetic nephropathy by follow-up of raised proteinuria also peaks at 11-15 years.

3. Hyperfiltration is seen in significant number of NIDDM patients. 29% of patients had hyperfiltration and 25% of them progressed to diabetic nephropathy irrespective of the initial urinary protein excretion.

4. The incidence of retinopathy is more than that of diabetic nephropathy in our series.

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