

A short-term evaluative study of diabetic nephropathy patients

Vaishya A¹, Mishra RN², Singh RG³ and Piplani KS⁴

¹ Research Scholar, ³ Professor, Deptt. of Nephrology, ² Professor, Division of Biostatistics, ⁴ Research Scholar, Department of Community Medicine, IMS, BHU, VARANASI-221005 (UP) INDIA

ABSTRACT

Background: Rising diabetes incidence globally and consequently diabetic nephropathy is a major concern. Being chronic disease patients are continuously monitored. Clinical improvement of major sign/symptoms in short course of therapy may lead to satisfaction of the patient's that will increase better compliance to the treatment.

Objective: To evaluate signs/symptoms and GFR status of diabetic nephropathy patient in short course of treatment therapy and nutritional management

Material & Methods: All 170 incident cases of diabetic nephropathy (DN) based on glomerular filtration rate and creatinine level registered on pre-fixed dates during May 2007 to May 2010, but 127 followed inclusion criteria. Patients were recorded for demographic, biological & biochemical characteristics and presenting major sign/symptoms at registration time; further, evaluated for presenting sign/symptoms after six months of medicine and dietary intervention.

Statistical Analysis: Statistical significance for association was tested by χ^2 (unrelated samples) and McNemar (related samples) and for the differences of number of signs/symptoms by Mann Whitney (unrelated samples) and Wilcoxon Signed Rank tests (related samples).

Results: No statistical association was seen between GFR status and presence of edema/swelling in any part of the body. After six months of treatment and dietary management, the edema/swelling presenting in 69.6% of the cases was found only in 33.3%. Pedal edema was found in 43.1%; while either eye lid or facial swelling was in 12.9% of the cases but after six months of drug treatment and dietary care these were present only in 18.6% and 3.9% cases respectively. GFR status of one third cases also improved after 6 months, while 57.8% were unchanged; very few (9.8%) deteriorated. The GFR improvement was more in cases reporting with GFR 60 and above.

Conclusion: Though, for the drug compliance and dietary intake patient's statement was believed, after six months of treatment and dietary care, edema/swelling, the major signs/symptoms of diabetic nephropathy that reduced significantly and moreover on an average one third reduction of all signs/symptoms among the cases may satisfy the cases resulting to better compliance to drug and dietary management. Better improvement in cases with higher GFR indicated that early detection of diabetic nephropathy cases is essential.

Key words: Diabetes, Diabetic Nephropathy (DN), Glomerular filtration rate (GFR), Renal Replacement Therapy (RRT), Creatinine, Hypertension

Introduction:

Non communicable diseases, like diabetes and coronary vascular disease (CVD) have increased several folds due to fast changing life style. India has the world's largest population suffering from diabetes¹. Worldwide estimates reveal that the people with diabetes will rise from 171 million in 2000 to 366 million by the year 2030². According to the Diabetes Atlas, in India 40 million people were estimated with diabetes in 2007 and predicted to rise to almost 70 million by 2025 making every 5th diabetic subjects in world to be an Indian³.

India with huge burden of diabetes having increasing vulnerability to the chronic complications such as diabetic nephropathy (DN) makes the populations more cripple. In India as per estimates, in 30 million diabetes patients DN is expected to develop in 6.6 million⁴. DN is characterized by persistent proteinuria (total urinary protein >0.5gm/24hour), arterial hypertension, declining

glomerular filtration rate (GFR) and plasma lipid abnormalities. The pandemic situation of diabetes and its micro-macro vascular complications calls for integration of health personnel and health care delivery system for prevention through various measures and interventions like increasing awareness towards the disease, changing life style and seeking medical care.

Treatment intervention in diabetic nephropathy includes glycaemic control, treatment of hypertension, hyperlipidemia, and protein restriction, cessation of smoking as well as renal replacement therapy⁵. The role of dietary management (in terms of protein restriction) along with drug therapy to prevent or to slow down further damage of kidney due to diabetes is well recognized. Associated major symptoms, if disappear, may have better prognostic value in the mind of the

Correspondence Address:

Archana vaishya, Research Scholar, Department of Nephrology Institute of Medical Sciences, Banaras Hindu University, Varanasi.
Email ID: arch_phd@rediffmail.com

patient and satisfying them with better compliance to treatment.

Objective:

To evaluate signs/symptoms and GFR status of diabetic nephropathy patient in short course of treatment therapy and nutritional management

Material and Methods:

It is a six months mid term evaluation as being the part of one year hospital based prospective study to evaluate the outcome of sign/symptoms in diabetic nephropathy patients managed by drug and dietary intervention protocol (Annexure-I). Study carried in the department of Nephrology, Institute of Medical Sciences, BHU on patients reporting on prefixed two OPD dates during May 2007 to May 2010. The follow up was on quarterly basis. The drug and dietary intervention varied from case to case during follow up depending upon the case condition. The dietary data was assessed on weekly basis. A designed diet diary was given to the patient and was assigned the dates on which the diet taken on 24 hours were recorded by the patient. The average of diet of all such dates was considered for dietary evaluation. The proportion 50% that gives the maximum sample size was considered to estimate the sample size within the confidence limit of estimate 40% to 60% and was calculated as 100. Assuming 20% of case may lost to follow, 125 cases was decided to follow to get a sample of 100 at the end.

Inclusion criteria: Patient with serum creatinine up to 5mg/dl, GFR >15 ml/minute and urinary protein >500 mg/day.

Exclusion criteria: Patients with GFR<15 or requiring dialysis or put on renal replacement therapy (RRT). Initially as per protocol all 170 patients attending Nephrology OPD were registered out of which 127 diabetic nephropathy patients followed the inclusion criteria for the present study. Out of 127, only 102 cases remain under follow up till six months. The cases according to their condition had been advised to follow the treatment and diet. The patients were categorized for their blood pressure as normal, pre-hypertensive, hypertension stage-I and stage-II⁶. Sex specific GFR was calculated following the standard formula⁷ as below:

$$GFR_{\text{male}} = \frac{(140 - \text{Age}) \times \text{Weight}}{72 \times \text{Creatinine (mg/dl)}}$$

$$GFR_{\text{female}} = \frac{(140 - \text{Age}) \times \text{Weight}}{72 \times \text{Creatinine (mg/dl)}} \times 0.85$$

Detailed systematic medical examination including age, sex, height and weight was carried. In addition to biochemical parameters estimation, detailed symptoms of micro vascular complications was recorded at base line and after the six months of drug therapy and nutritional management. For convenience in some tables and the text the term pre and post have also been used for base line and after six months of follow up.

Statistical Analysis:

The data was analyzed by SPSS, 16.0 versions. The cases under follow up till six months were initially compared for the demographic and biological characteristics as well as presenting major signs/symptoms with those who were lost to follow up using χ^2 with or without Yates correction depending on the situation and Mann Whitney (U) tests. The results presented are in percent, average with standard deviation (SD) for the number of signs/symptoms. For the signs/symptoms evaluation McNemar test was calculated. The change in number of signs/symptoms after six months was assessed by Wilcoxon Signed Rank Test (asymptotic Z test).

Results:

Out of 127 cases under follow up, 102 (80.32%) completed six months follow up (3 expired and 22 did not turn up). The base line demographic (age and sex) and biological/biochemical parameters (blood pressure, fasting blood sugar, GFR and creatinine) of those under follow up and lost to follow up were statistically similar (Table-1). The baseline distributions of number of signs/symptoms presenting among those under follow up and lost to follow were also similar (Table-II).

Though, presenting signs/symptoms of edema/swelling in any part of the body was comparatively lesser in patients with GFR 60-90, no statistical association was found (Table-III) indicating signs/symptoms may not be the predictor for GFR.

Signs/symptoms of edema and swelling had also develop to some absenting at base line but during the follow up as indicated in table-IV, at base line 69.6% had edema/swelling, but after six months of treatment and dietary management it was only 33.3% cases which was significantly lower (p<0.001).

Specific signs/symptoms at base line and after six months related to peripheral edema are represented in

table-V. At base line pedal edema was present in 43.1% of the cases that lowered significantly and was found only in 18.6% of the cases; while eye lid/facial swelling at base line was present in 12.9% of the cases that reduced and remained in only 3.9% of the cases after six months of treatment and dietary care.

Table-VI reveals evaluation of GFR status of the cases under follow up. In total 32.4% cases improved for their GFR, while 57.8% were stable; 9.8% cases were also found to deteriorate for their GFR. The improvement of GFR was in about more than 50% of the cases presented with GFR 60-90, while quarter to nearly one third with GFR 15-29 and 30-59. Compared to cases of GFR category 15-29, prognosis was significantly better in those with GFR category 60-90; while almost similar in GFR category 30-59.

Table I: Base line profile of the patients under six months follow up and lost to follow

Parameters	Patients under follow up (n = 102)		Patients lost to follow up (n = 25)		Comparison (χ^2 & p value)	
	No	%	No.	%		
Age (Yrs.)	< 50	18	16.5	3	2.05, df=3, 0.56	
	50-59	34	35.4	11		44.0
	60-69	35	32.3	6		24.0
	= 70	15	15.7	5		20.0
Sex	Male	21	19.7	4	0.27, df= 1, 0.61	
	Female	81	80.3	21		84.0
Blood Pressure	Normal	18	18.1	5	0.50, df=3, 0.92	
	Pre-hypertensive	22	20.5	4		16.0
	Hypertension Stage-I	40	40.2	11		44.0
	Hypertension Stage-II	22	21.3	5		20.0
Fasting Blood Sugar	Normal	44	43.1	10	1.75, df=1, 0.671	
	Hypo	4	3.9	0		0.0
	Hyper	50	49.0	12		48.0
	Not done	3	3.9	2		8.0
GFR	15 -29	43	42.2	11	0.80, df=2, 0.671	
	30 - 59	45	43.1	12		48.0
	60 - 89	15	14.7	2*		12.0
Creatinine	Normal	34	33.3	3*	4.07, df=1, 0.044	
	Above Normal	68	66.7	21		87.5

* One case could not be assessed ** to calculate χ^2 hypo and hyper frequencies merged together due to being small expected cell frequencies and not done were excluded. Yates correction made if expected cell frequency less than 5.

Table-II: Comparison of base line signs/symptoms of patients under 6 months follows up and lost to follow

Signs/Symptoms	Mann Whitney Test (Asymptotic Z and p values)	
	Z	P
Pedal edema	1.714	0.086
Generalized swelling (eye lid or facial swelling)	0.281	0.778

Table-III: Relation of oedema/swelling with GFF

GFR at the Time of Registration	Oedema/Swelling			
	Absent		Present	
	No.	%	No.	%
15-29	12	27.9	31	72.1
30-59	13	29.6	31	70.5
60-90	6	40.0	9	60.0
Total	31	30.4	71	69.6
0.80, df = 2, p = 0.672				

Table IV: Distribution of number of signs/symptoms (edema/swelling) present in patients at base line and at six months of follow up

All signs/symptoms combined	Base line		After six months	
	No.	%	No.	%
0	31	30.4	68	66.7
1	34	33.3	20	19.6
2	25	24.5	14	13.7
3	11	10.8	--	--
4	1	1.0	--	--
Mean \pm SD	1.19 \pm 1.02		0.47 \pm 0.73	
Wilcoxon Signed Rank Test; (Asymptotic Z value = 5.82; Asymptotic p value = 0.000)				

Table-V: Signs and symptoms at base line and after 6 months of treatment followed by drugs & dietary intervention

Signs/ Symptoms	Pre/ Post*	Signs/Symptoms		McNemar	
		Absent (%)	Present (%)	χ^2	P value
Pedal edema	Pre	56.9	43.1	17.45	0.000
	Post	81.4	18.6		
Generalized swelling (eye lid or facial swelling)	Pre	87.1	12.9	6.20	0.013
	Post	96.1	3.9		

* Some of the cases who had no Edema/Swelling may have developed

Table VI: Status of GFR after six months of treatment and nutritional management

GFR at the Time of Registration	GFR status after six month						Total	
	Unchanged		Improved		Deteriorated		No.	%
	No.	%	No.	%	No.	%		
15-29	26	60.5	11	25.6	6	14.0	43	100.0
30-59	27	61.4	14	31.8	3	6.8	44	100.0
60-90	6	40.0	8	53.3	1	6.7	15	100.0
Total	59	57.8	33	32.4	10	9.8	102	100.0
Between GFR	15-29 and 60-90			30-59 and 60-90				
χ^2	3.89			2.21				
df	1			1				
P*	0.049			0.137				

* Calculated between improved GFR and either unchanged or deteriorated

Treatment Protocol

An nexure-I

Components	Prescribed drugs either single or in combination	Dose/day
Blood Pressure	Amlodipine	2.5-15 mg
	Chloroquinehydrochloride	0.1-0.6 μ gm
	ACE Inhibitors- Ramipril	2.5-30 mg
	ARBs – Telmisartan	20-300 mg
	Torsemide	10-100 mg
	Hydralazine	80-100 mg
	Metoprolol	25-200 mg
	Aspirin (as antiplatelets)	75-150 mg
	Atorvastatin (Lipid lowering agent)	10-80 mg
Blood Sugar, if		
Hyperglycemia	Glycipride	1- 4 mg in divided dose
	Metformin	0.5 gm -2 gm in divided dose
hypoglycemia	Blood Glucose supplementation	As per requirement
GFR ml/min, if		
< 30		Normal prescribed drugs
30 -60		70% dose of prescribed drugs
= 60		50% dose of prescribed drugs

Nutritional Protocol

Nutrients	Requirement
Calorie	30 – 35 kcal/kg body weight
Protein	0.8 gm/kg body weight / (0.6gm as GFR reduces)
Fat	50 – 70 gm/day (10 – 12% of Kcal)
CHO	170 – 250 gm/day (60% of Kcal)
Na	2.3 gm/day
K	< 40 mmol/day
PO ₄	500 – 1000 mg/day

Discussion:

The changing life style throughout the world has led to continuous rise of diabetes cases and consequently to diabetic nephropathy cases. Uncontrolled blood sugar and blood pressure mainly cause early incidence of diabetic nephropathy. The suggested initial therapy in diabetic nephropathy is with ACE or ARBs and if after 4-6 weeks sufficient blood pressure reduction do not occur additional pharmacological therapy is indicated; none the less is the dietary management. The short term assessment to judge the prognosis for further modifications is always required in such chronic diseases. The basis of assessment for clinicians is GFR and levels of some biochemical values; however, for patients it is the disappearance of some major sign/symptoms for treatment seeking behavior and drug adherence. This study is a short term evaluation of diabetic nephropathy patients.

The base line demographic, biological characteristics as well as major presenting signs/symptoms of the patients (102) completing six months follow up were statistically similar to those who lost to follow (Table-I and II).

Table-III indicating no association between GFR and presence or absence of signs/symptoms of edema/swelling suggests the clinicians are not to judge improvement of kidney function on the basis of disappearance of signs/symptoms rather on GFR level; the clinical improvement of edema and swelling could be also due to intervention of diuretics. However, it is important on the part of patients; they might assess themselves for better prognosis that may lead them for better drug adherence and dietary care.

Presence of edema/swelling in significantly ($p < 0.001$) much less cases (33.3%) after a six month of treatment and dietary management compared to 69.6% at the

time of registration indicates that the patients may feel improvement of their kidney dysfunction leading them to satisfaction of better recovery and consequently to better adherence to drug and dietary care (Table-IV), though it is not the reality of improved kidney function.

At the time of registration pedal edema presented was highest in 43.1% cases; while eye lid/facial swelling was in 12.9% cases. After the drug and dietary compliance pedal edema was presenting only in 18.6% and eye lid/facial swelling in 3.9% of the cases. A significant change is a good indicator to the patient's satisfaction.

Though, studies enumerating exhaustively sign/symptoms are limited, however some had precedence not on diabetic nephropathy rather among diabetic cases. Khandelwal et al (2011) reported cardiovascular autonomic neuropathy that varied from 6.49% to 47.41%. Karmakar et al (2011) on cases of diabetes type-II patients indicated that 21 patients (21%) had proteinuria and 31 (31%) had neuropathy. Both were present in 16% patients and absent in 64% cases. The overall prevalence of neuropathy and proteinuria among study subjects was 36%. Isolated peripheral neuropathy was found in 9% patients, isolated autonomic neuropathy was found in 7% patients, and both were present in 15% cases. Hall et al (2012) investigated type-II diabetic patients after intervention and found that hazard ratios for macrovascular events, OGLD versus insulin, were 0.53 (95%CI: 0.42, 0.69) from one baseline treatment, 0.85 (95% CI: 0.70 1.04) from two and 1.07 (95% CI: 0.50, 2.30) from three, with no difference in risk of microvascular disease in any comparison.

As regards to clinician evaluation, as indicated in Table-VI, in total only 9.8% cases deteriorated for their GFR while 32.4% cases improved and 57.8% were stable to their GFR category. The improvement was in more than 50% cases with GFR 60-90, while only in quarter to nearly one third with GFR 15-29 and 30-59 respectively. Compared to GFR category 15-29, prognosis was significantly more in those with GFR category 60-90; while almost similar in GFR category 30-59. This indicates the early stage reporting and adherence to drug and dietary care may have better prognosis and satisfying to both clinician and the patients.

Conclusion:

Though, for the drug compliance and dietary intake patient statement was believed, after six months of treatment and dietary care, edema/swelling, the major

signs/symptoms of diabetic nephropathy that reduced significantly and moreover on an average one third reduction of all sign/symptoms among the cases may satisfy the cases resulting to better compliance to drug and dietary management. Better improvement in cases with higher GFR indicated that early detection of diabetic nephropathy cases is essential.

Acknowledgement:

Authors are thankful to the patients who cooperated in this study for their help and consent.

References:

1. United States Renal Data System (USRDS). Annual Data Report, Bethesda, MD; National Institute of Diabetes & Digestive & Kidney Diseases: National Institutes of Health, U.S., Department of Health & Human Services: 2007.
2. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 & projection for 2030. *Diabetes Care*. 2004; 27 (5): 1047-53.
3. Sicree R, Shaw J, Zimmet P. Diabetes & impaired glucose tolerance; In. *Diabetes Atlas*, Inter National Diabetes Federation Third Edition: Edited by Gan D. International Diabetes Federation, Belgium. 2006; 15-103.
4. Hossain P, Kawar B, Nahas MEL. Obesity & Diabetes in the developing world- A growing challenge. *N Engl j med*. 356; (3): 213-215.
5. Ayodele OE, Alebiosu CO, Salako BL. Diabetic nephropathy – a review of the natural history, burden, risk factors and treatment. *J Natl Med Assoc*. 2004; 96(11): 1445-54.
6. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, & Treatment of High Blood Pressure: The JNC 7 Report. 2003: 21; 289 (19); 2560-71.
7. Cockcroft D, Gault M. Prediction of creatinine clearance from serum creatinine. *Nephron*. 1976; 16: 31-41.
8. Khandelwal E, Jarval AK and Deepak KK. Pattern and prevalence of cardiovascular autonomic neuropathy in diabetics visiting a tertiary care referral center in India. *Indian Journal of Physiol. Pharmacol*. 2011, April-June; 119-27.
9. Karmakar RN, Khandakar MR, Gangopadhyay, Ghosh K, Babu AS. Albuminuria and neuropathy in newly detected diabetics: profile and correlation. *Indian Journal of Med. Assoc*. 2011, Jun; 109 (6): 396-9.
10. Hall GC, McMohan AD, Carroll D and Home PD. Macrovascular and microvascular outcomes after beginning of insulin versus additional oral glucose-lowering therapy in people with type 2 diabetes: an observational study. *Pharmacoepidemiol Drug saf*. (2012), Mar; 21 (3): 303-13.