THE ROLE OF DURATION OF DIABETES IN THE DEVELOPMENT OF NEPHROPATHY

Ishwar Sidappa Hasabi[1], Basith Lateef Kardkal[2], Uday Subhash Bande[3]

[1]Professor and HOD, Department of General Medicine, Karnataka Institute of Medical Sciences, Hubli, Karnataka.
[2]Physician, Department of General Medicine, Government Hospital, Manvi, Raichur.
[3]Associate Professor, Department of General Medicine, Karnataka Institute of Medical Sciences, Hubli, Karnataka.

ABSTRACT

BACKGROUND

Diabetes has now become the most common single cause of end-stage renal disease. Diabetic Kidney Disease (DKD) is a life-threatening and irreversible microvascular complication characterised by presence of persistent proteinuria, hypertension and progressive decline in renal function. Early detection and risk reduction measures can prevent diabetic nephropathy. Screening for microalbuminuria will allow early identification of patients with nephropathy provide an opportunity for early treatment, which has been shown to preserve renal function and thus prevent morbidity and mortality from diabetic nephropathy.

The aim of the study is to study the relation between duration of diabetes and nephropathy.

MATERIALS AND METHODS

120 patients with type 2 diabetes mellitus admitted to medical wards, KIMS, Hubli, over a period of one year satisfying the inclusion and exclusion criteria were enrolled for the study. 40 normal healthy adults were included in the control group. It's a cross-sectional study and patients were enrolled by random sampling method. All the selected patients were subjected to detailed history and complete physical examination and data collected was noted in a predesigned pro forma.

RESULTS

Study participants were subdivided based on duration of diabetes into <5 years, 5-10 years and >10 years. Their mean age of onset of diabetes was 54.5 (± 10) years. Microalbuminuria was present in 45% (n=54) of diabetics, retinopathy 35.8% (n=43) and both increased with increase in duration of diabetes (p value 0.003 and 0.001, respectively) (Table 3 and 4). Prevalence of hypertension was 51.7% in present study group and was significantly associated with duration of diabetes.

CONCLUSION

This study highlighted the prevalence of microalbuminuria and retinopathy in type 2 diabetes subjects. Microalbuminuria increases with increase in duration of diabetes. Screening for microalbuminuria will allow early detection of patients with nephropathy.

KEYWORDS

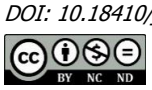
Diabetes, Duration of Diabetes, Nephropathy.

HOW TO CITE THIS ARTICLE: Hasabi IS, Kardkal BL, Bande US. The role of duration of diabetes in development of nephropathy. J. Evid. Based Med. Healthc. 2017; 4(95), 6017-6021. DOI: 10.18410/jebmh/2017/1212

BACKGROUND

Diabetes mellitus now ranks as the primary cause of End-Stage Kidney Disease (ESKD) requiring chronic renal replacement therapy. Decreased GFR and albuminuria are indicators of major health outcomes of this condition including End-Stage Renal Disease (ESRD) and death.[1] Studies have demonstrated that the factors strictly correlated to the progression of nephropathy in diabetic patients are arterial blood pressure, glycaemic control, lipid levels, proteinuria levels, obesity, anaemia and cigarette smoking with most of these critically influencing mortality.[2]

Financial or Other, Competing Interest: None.
Submission 21-11-2017, Peer Review 05-12-2017,
Acceptance 12-12-2017, Published 23-12-2017.
Corresponding Author:
Dr. Basith Lateef Kardkal,
Physician, Department of General Medicine,
Government Hospital Manvi, Raichur.
E-mail: basithl@yahoo.com
DOI: 10.18410/jebmh/2017/1212



It is estimated that approximately 285 million people or 6.4% in the age group 20-79 will have diabetes worldwide in 2010. About 70% of these live in low- and middle-income countries. The worldwide estimate is expected to increase to some 438 million or 7.7% of the adult population by 2030. The highest prevalence will continue to be in North America and Caribbean, the Middle East and North Africa and South East Asia.[3]

Type 2 diabetes is far more prevalent than type 1 diabetes. Many patients with type 2 diabetes have ESRD.[4]

Chronic Kidney Disease (CKD) is a worldwide public health problem with adverse outcomes of kidney failure, Cardiovascular Disease (CVD) and premature death.[5,6]

Hyperglycaemia, increased blood pressure levels and genetic predisposition are the main risk factors for the development of diabetic nephropathy. In patients with type 2 diabetes, screening should be performed at diagnosis and yearly thereafter. Patients with micro- and macroalbuminuria should undergo an evaluation regarding the presence of comorbid associations, especially retinopathy and macrovascular disease.[7] In addition to its

being the earliest manifestation of nephropathy, albuminuria is a marker of greatly increased cardiovascular morbidity and mortality.[8]

Duration of diabetes is a very important factor in the development and severity of diabetic nephropathy.[9] If the relation between duration of diabetes and development of diabetic nephropathy could be established, screening of early signs of nephropathy provide an opportunity for early treatment, which has been shown to preserve renal function ensuring that patients with diabetes will live longer and have better lives.

Hence, this study aims at studying the role of duration of diabetes in development of nephropathy in patients with type 2 diabetes mellitus thereby reassessing the need for early recognition and more aggressive management of the disease.

MATERIALS AND METHODS

A total of 120 patients with type 2 diabetes mellitus admitted to medical wards, KIMS, Hubli, over a period of one and a half year satisfying the inclusion and exclusion criteria were enrolled for the study. 40 normal healthy adults were included in the control group. It is a cross-sectional study and patients were enrolled by random sampling method. All the selected patients were subjected to detailed history and complete physical examination and data collected was noted in a predesigned pro forma.

Inclusion and Exclusion Criteria

Patients who developed diabetes after 30 years of age were considered to have type 2 diabetes and divided with diabetes of less than 5 years duration, 5-10 years duration and more than 10 years duration will be selected. Diabetic patients with microproteinuria were considered to have nephropathy. Patients with type 1 diabetes, patients having microalbuminuria due to other disease and patients with debilitating disease were excluded. Weight of the subjects were measured as weight in kilograms using a digital weighing scale. Microalbuminuria was assessed on a spot sample of urine using a microalbumin test kit. Serum creatinine of the patients was measured in the biochemistry laboratory of KIMS, Hubli. Blood samples were collected under aseptic precautions after obtaining informed consent for estimation of blood urea and serum creatinine and other investigations.

Statistical Analysis- All data is expressed as mean ± SD. The results were analysed by calculating percentages, Chi-square test and Student's t-test. A p value of less than 0.05 was considered statistically significant.

RESULTS

Present study included participants 64 males and 56 females with mean (±SD) age 54.5 (±10) years. 120 patients with type 2 diabetes mellitus were divided based on duration of diabetes into <5, 5-10 and >10 years with 40 subjects in each category. In present study, prevalence of hypertension was 51.7% (n=62), 28.3% were smokers. Based on complication of diabetes, the prevalence of retinopathy was 35.8% (n=43), CVS disease was 23.3%, stroke 8.3% and dyslipidaemia 21.7%, diabetic foot 4% and skin manifestation 7%. Mean BMI 25.7, mean HbA1c was 9.8%. Blood urea was 54.6, serum creatinine was 2.6 and urine albumin was 398. Hypertension was associated with microalbuminuria was significant with p value <0.001*. Retinopathy was associated with microalbuminuria and was significant with p value 0.001 (Table 1). BMI, haemoglobin, HbA1c, blood urea, creatinine and urine albumin increased with duration of diabetes and was significant (Table 2). When association between microalbuminuria and duration of diabetes mellitus was assessed, it was 27.5% in <5 years, 42.5 in 5-10 years and 65% in >10 years of diabetes duration. It increased with increase in duration of diabetes and was significant 0.003* (Table 3).

Sl. No.	Characteristics	Albuminuria Status			Chi-Square Value, df	p Value
		Normal n (%)	Microalbuminuria n (%)	Macroalbuminuria n (%)		
1.	**Smoking Status**					
	Present	18 (52.9)	3 (8.8)	13 (38.2)	0.24, 2	0.88
	Absent	48 (55.8)	9 (10.5)	29 (33.7)		
2.	**Hypertension**					
	Present	23 (37.1)	5 (8.1)	34 (54.8)	22.38, 2	<0.001
	Absent	43 (74.1)	7 (12.1)	8 (13.8)		
3.	**Retinopathy**					
	Present	17 (39.5)	2 (4.7)	24 (55.8)	13.12,2	0.001
	Absent	49 (63.6)	10 (13)	18 (23.4)		
4.	**Dyslipidaemia**					
	Present	13 (50)	2 (7.7)	11 (42.3)	0.83, 2	0.65
	Absent	53 (56.4)	10 (10.6)	31 (33)		

Table 1. Association between Albuminuria and other Study Variables

Sl. No.	Characteristics	Duration of Diabetes Mellitus in Mean Years with Standard Deviation (SD)			F Value, df	p Value
		<5	5-10	>10		
1.	Age in years	55.0 (10.7)	53.7 (10)	54.8 (9.5)	0.21, 2	0.81
2.	BMI	24.4 (3.7)	26.8 (4.2)	26.1 (3.2)	4.57, 2	0.01
3.	Haemoglobin in g/dL	11.3 (1.9)	9.8 (2.0)	9.0 (1.9)	14.05, 2	<0.001

4.	HbA1c in %	9.1 (3.5)	9.4 (2.6)	10.7 (15.6)	5.69, 2	0.05
5.	Blood urea in mg/dL	42.1 (35)	47.6 (38.7)	74 (41.9)	18.12, 2	<0.001
6.	Creatinine in mg/dL	1.5 (1.4)	2.9 (5.3)	3.5 (2.5)	22.66, 2	<0.001
7.	Urine albumin in mg/dL	107.4 (188.4)	252.3 (325.7)	834.4 (905.8)	22.82, 2	<0.001

Table 2. Comparison of Study Participants Based on Duration of Diabetes Mellitus with Various Study Parameters

Duration of Diabetes Mellitus in Years	Microalbuminuria		Chi-Square Value, df	p Value#
	Yes, n (%)	No, n (%)		
<5	11 (27.5)	29 (72.5)	11.51, 2	0.003*
5-10	17 (42.5)	23 (57.5)		
>10	26 (65)	14 (35)		
	54 (45)	66 (55)		

Table 3. Association between Microalbuminuria and Duration of Diabetes Mellitus

Duration of Diabetes Mellitus in Years	Retinopathy		Chi-Square Value, df	p Value#
	Yes, n (%)	No, n (%)		
<5	7 (17.5)	33 (82.5)	14.20, 2	0.001*
5-10	13 (32.5)	27 (67.5)		
>10	23 (57.5)	17 (42.5)		
Total	**43 (35.8)**	**77 (64.2)**		

Table 4. Association between Retinopathy and Duration of Diabetes Mellitus

Characteristics	Normal	Duration of Diabetes Mellitus in Mean Years with Standard Deviation (SD)			F Value, df	p Value
		<5	5-10	>10		
Age in years	45.0 (9.6)	55.0 (10.7)	53.7 (10)	54.8 (9.5)	9.05, 3	<0.001*
Urea in mg/dL	23.5 (6.9)	42.1 (35.0)	47.6 (38.7)	74.0 (41.9)	15.33, 3	<0.001*
Creatinine in mg/dL	1.04 (0.2)	1.53 (1.5)	2.89 (5.3)	3.53 (2.4)	5.68, 3	0.001*
Urine albumin in mg/dL	38.9 (84.93)	107.3 (188.4)	252.3 (325.7)	834.4 (905.8)	21.61, 3	<0.001*

Table 5. Comparison of Mean Age and Various Biochemical Test with Duration of DM in Overall Study Subjects

DISCUSSION

The classic description of diabetic nephropathy is of a progressive increase in proteinuria in people with longstanding diabetes followed by declining function that eventually can lead to end-stage renal disease. The rate of progression from normoalbuminuria to microalbuminuria then to overt nephropathy usually is slow, typically taking 5 years or longer to progress through each stage.[10]

Present study was conducted in 120 patients with type 2 diabetes mellitus. They were subdivided based on duration of diabetes into <5 years, 5-10 years and >10 years. Their mean age of onset of diabetes was 54.5 (±10) years. Microalbuminuria was present in 45% (n=54) of diabetics, retinopathy 35.8% (n=43) and both increased with increase in duration of diabetes (p value 0.003 and 0.001, respectively) (Table 3 and 4). Prevalence of hypertension was 51.7% in present study group and was significantly associated with duration of diabetes (p value 0.001) (Table 1). The mean (±SD) serum creatinine was 2.6 (±3.6) and blood urea was 54.6 (±40.8) and were significantly related to duration of diabetes (p<0.001) (Table 2). Mean HbA1c in present study participants was 9.8 (SD ± 9.3). HbA1c was correlated with duration of diabetes. It was statically significant (P=0.05) (Table 2).

Present study reported that as duration of diabetes increases, there was increase in prevalence of microalbuminuria. When association between duration of diabetes and microalbuminuria was assessed, it was present in 11 (27%) individuals with duration of diabetes <5 years 17 (42.5%) with 5-10 years and 26 patients (65%) with >10 years of duration of diabetes.

Similar results were obtained as in present study by Inassi J el at conducted study in 120 patients with type 2 diabetes. Number of subjects with proteinuria was 10 in <5 years, 12 in 5-10 years and 32 in >10 years. Proteinuria increased as duration of diabetes increased and was significant (p 0.001). It was observed that there was a significant relation between blood urea, serum creatinine, microproteinuria and blood pressure with the duration of diabetes.[9]

Results of the present study are comparable with the results obtained in a study conducted by Pasko et al.[11] The odds ratio for microalbuminuria became statistically significantly increased 16 years after the diagnosis of type 2 diabetes by which time 48.2% of patients had microalbuminuria.[11]

Brenhya et al[12] stated the frequency of heavy proteinuria showed a gradual increase from a frequency of 7.8% in study participants with diabetes duration of <1 year through 8.1% (in 2-5 years group), 14.5% (in the 6-10 years group), 33.3% (in the 11-15 years group) and 60.0% in the 16-20 diabetes duration group.

Chowta et al stated that in their study, four (7.4%) had microalbuminuria. Twenty four patients had duration of

diabetes between 5 and 10 years, among them 12 (50%) had microalbuminuria.[13] Balasubriya et al stated that the prevalence of nephropathy (microalbuminuria) in <1 year group was 18.8%, in 6-10 years group 21.2% and in the over 20 years group 25.4%.[14]

In a follow up study Viswanathan V et al in their study during median follow up of 11 years, 44.1 percent developed proteinuria at follow up in 2630 type 2 diabetics. They concluded patients with uncontrolled diabetes and increases in blood pressure are at high risk of developing nephropathy.[15]

Similar to present study, Unnikrishnan et al conducted a study in type 2 diabetic subjects selected from the Chennai Urban Rural Epidemiology Study (CURES). There was an increase in the prevalence of microalbuminuria with the increase in duration of diabetes.[16]

In present study, microalbuminuria was present in 45% of subjects. When association between microalbuminuria and duration of diabetes was assessed, it was present in 11 (27%) individuals with duration of diabetes <5 years, 17 (42.5%) with 5-10 years and 26 patients (65%) with >10 years of duration of diabetes. It was significantly associated with duration of diabetes with p value 0.003. (Table 3).

Pasko et al reported the odds ratio for microalbuminuria became statistically significantly increased 16 years after the diagnosis.[11]

In a similar study, Chowta et al stated that duration of diabetes had significant contribution for the development of microalbuminuria by prolonged exposure to hyperglycaemia-induced AGE product accumulations.[13]

Balasuriya et al studied the prevalence of nephropathy (microalbuminuria) in a subset of Sri Lankan population in <1 year group was 18.8%, in 6-10 years group 21.2% and in over 20 years group 25.4%.[14] In related study, Alwakeel et al concluded that diabetic nephropathy among Saudis tends to be progressive with GFR decline at a rate of 3.3 mL/year with doubling of serum creatinine.[17]

Present study found that retinopathy was prevalent in 35.8% (n=43) of study subjects (Table 1). There was a positive correlation between prevalence of retinopathy and duration of diabetes with p value 0.001.

Similar results were obtained in a study by Balasuriya et al reported a progressive rise in the number of retinopathy cases as the duration of diabetes increased.[14] Alwakeel et al also reported the progressors had a significantly higher prevalence of cataract, retinopathy, angina and neuropathy compared to non-progressors.[17] As reported by Rani et al, the prevalence of diabetic retinopathy was 17.6% in self-reported rural population with diabetes.[18]

Agarwal RP et al reported prevalence of micro and microvascular complications in 11,157 type-2 diabetic patients, retinopathy was found in 3621 (32.5%) patients.[19]

HbA1c was correlated with duration of diabetes, it was statically significant (Table 3). Islam et al in their study reported mean HbA1c of 10.07 ± 3.27% in diabetes group by use of multiple logistic regression analysis showed that the duration of DN (<3 years = 0 vs. ≥3 years = 1) is associated with sex, systolic BP, serum creatinine, HbA1c and duration of hypertension adjusting for other variables.[20]

Smoking was present in 34 (28.3%) of the individuals and absent in 86 (71.7%) of the individuals. In most of similar study, there were 39 (65%) smokers in the DN group and 24 (40%) smokers in the non-DN group. The average duration of smoking among the DN patients was 19.2 ± 4.80 years. A statistically significant relationship was found between DN and smoking (P=0.006).[4]

Hypertension was 51.7% in present study group and was positively correlated with albuminuria and statistically significant with p value of <0.001.

Similar to our findings, Nohman et al reported that the duration of DM and HTN were strong predictors for the development of DN (P=0.001).[18]

Cardiovascular disease was present in 28 (23.3%) individuals and absent in 92 (76.6%), stroke in 10 (8.3%) individuals and dyslipidaemia in 26 (21.7%) absent in 94 (78.3%) of the study population. There was no association with cardiovascular disease and duration and diabetes. Other complications such as stroke was present in 8.3% of individuals dyslipidaemia was 21.7%, diabetic foot was 3.3% and skin manifestation in 7 individuals (5.8%).

CONCLUSION

Diabetic nephropathy is a chronic complication of DM with a growing incidence. Therefore, it is essential to have a better understanding of it, especially in relation to prevention and aggressive management to avoid progression to ESRD. Endeavour should be made to control hyperglycaemia and hypertension tightly by appropriate therapeutic measures, so that the occurrence and worsening of the complications could be mitigated.

Control of modifiable risk factors, especially blood glucose and blood pressure should be optimised to reduce the risk of diabetic nephropathy.

Early diagnosis and multidirectional treatment constitute the only effective way of stopping the progression of kidney disease and improving prognosis. In clinical practice, the intensive treatment undertaken in the advanced disease may only slow down its progression. Further, prospective trials including patients with type 2 diabetes are needed to better assess the relationship between duration of diabetes and microalbuminuria.

REFERENCES

[1] Prakash J. Non-diabetic renal disease (NDRD) in patients with type 2 diabetes mellitus (type 2 DM). J Assoc Physicians India 2013;61(3):194-199.
[2] Liang S, Zhang XG, Cai GY, et al. Identifying parameters to distinguish non-diabetic renal diseases from diabetic nephropathy in patients with type 2 diabetes mellitus: a meta-analysis. PLoS One 2013;8(5):e64184.
[3] Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010;87(1):4-14.

[4] Ahmed MA, Kishore G, Khader HA, et al. Risk factors and management of diabetic nephropathy. Saudi J Kidney Dis Transpl 2013;24(6):1242-1247.
[5] Levey AS, Eckardt KU, Tsukamoto Y, et al. Definition and classification of chronic kidney disease: a position statement from Kidney disease: improving Global Outcomes (KDIGO). Kidney Int 2005;67(6):2089-2100.
[6] Introduction to Volume 1: CKD in the United States. American Journal of Kidney Diseases 2016:67(3):S1-S12.
[7] Gross JL, de Azevedo MJ, Silveiro SP, et al. Diabetic nephropathy: diagnosis, prevention and treatment. Diabetes Care 2005;28(1):176-176.
[8] Molitch ME, DeFronzo RA, Franz MJ, et al. Nephropathy in diabetes. Diabetes Care 2004;27 Suppl 1:S79-S83.
[9] Inassi J, Vijayalakshmy R. Role of duration of diabetes and development of nephropathy in type 2 diabetic patients. Natl J Med Res 2013;3(1):5-8.
[10] McFarlane P, Gilbert RE, MacCallum L, et al. Chronic kidney disease in diabetes. Can J Diabetes 2013;37(Suppl 1):S129-S136.
[11] Pasko N, Toti F, Strakosha A, et al. Prevalence of microalbuminuria and risk factor analysis in type 2 diabetes patients in Albania: the need for accurate and early diagnosis of diabetic nephropathy. Hippokratia 2013;17(4):337-341.
[12] Brenyah RC, Ephraim RKD, Owiredu WKBA, et al. Prevalence and determinants of proteinuria among type 2 diabetics in Kumasi, Ghana. Journal of Medical and Biomedical Sciences 2013;2(1):13-21.
[13] Chowta NK, Pant P, Chowta MN. Microalbuminuria in diabetes mellitus: association with age, sex, weight, and creatinine clearance. Indian J Nephrol 2009;19(2):53-56.
[14] Balasuriya BMAC, Sumanatilleke MR, Jayasekera TI, et al. Prevalence of micro and macrovascular complications of diabetes detected at single visit screening. Sri Lanka J Diabetes Endocrinol Metab 2012;2(1):17-20.
[15] Viswanathan V, Tilak P, Kumpatla S. Risk factors associated with the development of overt nephropathy in type 2 diabetes patients: a 12 years observational study. Indian J Med Res 2012;136(1):46-53.
[16] Unnikrishnan RI, Rema M, Pradeepa R, et al. Prevalence and risk factors of diabetic nephropathy in an urban South Indian population: the Chennai Urban Rural Epidemiology Study (CURES 45). Diabetes Care 2007;30(8):2019-2024.
[17] Alwakeel JS, Isnani AC, Alsuwaida A, et al. Factors affecting the progression of diabetic nephropathy and its complications: a single-center experience in Saudi Arabia. Ann Saudi Med 2011;31(3):236-242.
[18] Rani PK, Raman R, Chandrakantan A, et al. Risk factors for diabetic retinopathy in self-reported rural population with diabetes. J Postgrad Med 2009;55(2):92-96.
[19] Agrawal RP, Ola V, Bishnoi P, et al. Prevalence of micro and macrovascular complications and their risk factors in type-2 diabetes mellitus. J Assoc Physicians India 2014;62(6):504-548.
[20] Islam SM, Islam MS, Rawal LB, et al. Clinical profile of patients with diabetic nephropathy in a tertiary level hospital in Dhaka, Bangladesh. Arch Med Health Sci 2015;3(2):191-197.