A Study of Prevalence of Microalbuminuria and Diabetic Retinopathy in Rural Patients Presenting to a Tertiary Care Hospital in North India

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ABSTRACT

Introduction: Diabetic nephropathy is the leading cause of End Stage Renal Disease in the world, accounting for more than one third of the cases. Micro albuminuria is a marker of wide spread micro vascular damage in Type 2 Diabetes Mellitus and an earliest marker for nephropathy. The correlation between presence of overt proteinuria and proliferative diabetic retinopathy have been demonstrated in both Type 1 and Type 2 diabetic patients. There is an increasing evidence that micro albuminuria could be used as a marker for early diabetic retinopathy. However, this relationship has not been established in our setting. Hence, we planned to evaluate the prevalence as well as correlation of micro albuminuria and retinopathy in patients of Type 2 Diabetes Mellitus.

Material and Methods: 100 Type 2 diabetic patients willing to participate, were enrolled in the study after due approval from the Institutional Ethical committee. Prevalence of micro albuminuria was checked using Micral test. Body Mass Index and Glycosylated Hemoglobin were also measured. Patients were evaluated by direct and indirect ophthalmoscopy to look for evidence of retinopathy.

Results: 56% patients were male with majority of them (70%) were in the age group of 40-60 years. In 39% patients, duration of diabetes was less that 5 years and equal percentage of patients had micro albuminuria. 45% patients showed signs of diabetic retinopathy, whereas, both micro albuminuria and retinopathy were observed in 32% of patients ($p < 0.001$). Compared to overall prevalence of micro albuminuria and retinopathy, patients with age more than 50 years showed higher prevalence of 51.61% and 56.45% ($p=0.001$) respectively. Micro albuminuria (52.45%) and diabetic retinopathy (57.37%) were more likely with duration of diabetes above 6 years ($p=0.001$). Other factors which were statistically significant were Glycosylated Hemoglobin (HbA1c) more than 7% and Body Mass Index (BMI) >25kg/m^2.

Conclusion: The study showed that there is significant correlation between the presence of micro albuminuria and diabetic retinopathy. Several factors like increase in age, duration of diabetes, HbA1c levels on admission and body mass index are associated with increased prevalence of micro albuminuria and diabetic retinopathy.

Key words: Micro Albuminuria, Diabetic Retinopathy, Micral Test

INTRODUCTION

Diabetes has reached epidemic proportions in India in the 21st century, with 65.1 million people suffering from diabetes. According to International Diabetes Federation (IDF), by 2035 nearly 109 million people are likely to be affect from diabetes in India.[1,2] Diabetes is characterized by metabolic abnormalities and long term microvascular and macrovascular complications. With the increase prevalence of diabetes, there is a significant increase in the microvascular complication like retinopathy, nephropathy, neuropathy, coronary heart diseases and cerebrovascular accidents. These microvascular complications are linked to the duration of diabetes, poor glycemic control and increased BMI. Diabetic retinopathy is one of the leading causes of blindness in the world that increases the chances of losing sight by about 25 times as compared to normal individual.[3] Diabetic nephropathy occurs in as many as 30% of type I diabetes mellitus patients and 25% of type II diabetes mellitus patient. It is a dreaded disease with progressive and continuous deterioration in glomerular function. In the early phase of diabetic nephropathy, there is a rise in urinary excretion of albumin i.e. microalbuminuria which is detectable only by use of sensitive assay for urinary albumin. At this stage, urine is negative for macroalbumin and renal function is normal by standard clinical tests. The presence of microalbuminuria precedes the development of overt diabetic nephropathy by 10 to 15 years. It is at this stage that one can hope to reverse diabetic microvascular complications and prevent its progression. In type 2 diabetic patients, 20-40% with microalbuminuria progress to overt nephropathy and 20 years later, approximately 20% develop end stage renal failure.[4] Diabetic Retinopathy is responsible for 4.8% of the 37 million cases of blindness throughout the world.[3] The concordance of microalbuminuria and diabetic

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retinopathy has well reported in type 1 diabetes; however, for type 2 diabetes, there is paucity of data. Present study primarily reports the prevalence of microalbuminuria among persons with Type 2 Diabetes Mellitus and evaluates its role as a risk factor for the presence of diabetic retinopathy.

MATERIAL AND METHODS

The study was conducted at a tertiary care medical college in North India. 100 Type 2 diabetic patients willing to participate, were enrolled in the study after due approval from the Institutional Ethical committee. Known as well as newly diagnosed patients from Outpatient department, Emergency department (ED), Inpatient department (IPD) and Intensive care units (ICU) were enrolled in the study. Diabetes was defined on the basis of following American Diabetes Association (ADA)[5] criteria:

- Fasting blood glucose ≥126 mg/dl (7.0mmol/l). Fasting is defined as no caloric intake for at least 8 hours. (or)
- HbA_{1C}≥6.5% (48mmol/mol) (or)
- Two-hour plasma glucose ≥200mg/dl (11.1mmol/l) during an oral glucose tolerance test (OGTT) (or)
- In a patient with classical symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200mg/dl (11.1mmol/l)

Every subject was informed about the study and a written consent was taken from the subjects. Pregnant woman and subjects with Type 1 Diabetes Mellitus, hypertension (Primary or secondary), macroalbuminuria, congestive cardiac failure, urinary tract infection, primary kidney disease or overt diabetic nephropathy were excluded. For all the included patients detailed history (age, sex, age of onset, duration of diabetes, presenting complaints, drug history including OHA/ Insulin, family history of diabetes, personal history), physical examination was recorded and patients were subjected to following investigations: Microalbuminuria estimated by MICRAL test, Fasting blood sugar and Postprandial blood sugar, Glycosylated hemoglobin (HbA1c), Blood urea, Serum creatinine, Fasting lipid profile, Urine routine examination and Electrocardiogram. Ultrasonography of the abdomen, Echocardiogram and Chest X-ray was done in selected cases only. Detailed ophthalmic examination (visual activity, slit lamp examination, fundus examination) was done in every included patient. The MICRAL test is an immunospecific dipstick for detection of low concentrations of albumin in urine (microalbuminuria). The test is primarily intended to be used for screening in an ambulatory settings, however, its utility in detecting microalbuminuria in selected patients compared to albumin creatinine ration has been validated by many studies.[6,7,8] In a study done by Jensen et al[6], the sensitivity and specificity of MICRAL test as calculated from the pooled data were 83.2% and 92.3%, respectively. The test has a high positive predictive value and a low negative predictive value. However, that varies according to the prevalence of microalbuminuria in the selected population. Statistical analysis was done using statistical software SPSS. The patients' demographic data and baseline characteristics were presented using means, standard deviation and percentage. Chi-square test was employed to test the association between microalbuminuria and retinopathy in type 2 diabetic patients. The magnitude of the difference in proportion of diabetic retinopathy between type 2 diabetes with micro- and normoalbuminuria was presented along with 95% confidence interval.

RESULTS

We studied a total number of 100 patients of Type 2 Diabetes Mellitus. In our study population, 56% were males with majority of patients (70%) were in the age group of 40-60 years. The mean age of the study population was 56.31 years with SD ±10.49 years. Over all 39% of patients had microalbuminuria. 45% patients showed signs of diabetic retinopathy only, whereas, both microalbuminuria and retinopathy were observed in 32% of patients (p <0.001). The mean duration of diabetes was 7.78 years with 39% having duration of diabetes less than 5 years. Majority of patients i.e. 78%, had a normal BMI. Most patients (56%) in the study population had uncontrolled blood sugars with HbA1c value more than 7% (Table-1). On correlating HbA1c level with microalbuminuria and retinopathy, we observed that with HbA1c level >7%, microalbuminuria was seen in 51.78% patients (29/56) whereas retinopathy was found in 62.5% patients (35/56) (p=0.001). Compared to overall prevalence of microalbuminuria and retinopathy, patients with age more than 50 years, showed higher prevalence of 51.61% (32) and 56.45% (35) respectively (p=0.001). Microalbuminuria (52.45%) and diabetic retinopathy (57.37%) were more likely with duration of diabetes above 6 years (p=0.001). Microalbuminuria and retinopathy were found in 59.09% (p=0.024) and 68.18% (p=0.059) of the diabetic patients respectively having BMI >25 kg/m^2

Category		No. of Patients (n=100)	Percentage (%)
Gender	Male	56	56
	Female	44	44
Age (years)	40-50	38	38
	51-60	32	32
	61-70	20	20
	>70	10	10
Microalbuminuria	-	61	61
	+	39	39
Retinopathy	-	55	55
	+	45	45
Duration of DM (Years)	≤5	39	39
	6 -10	30	30
	11-15	19	19
	>16	12	12
Body mass index (Kg/m^2)	<25	78	78
	>25	22	22
HbA1c (%)	<6.5	22	22
	6.5-7	22	22
	7.1-7.5	16	16
	>7.5	40	40

Table-1: Baseline characteristics of the study population

Category		Number of Patients (N=100)	Microalbuminuria		Retinopathy	
			-	+	-	+
Age in years	40-50	38	31	07	28	10
	51-60	32	21	11	19	13
	61-70	20	08	12	8	12
	> 70	10	01	09	-	10
Duration of Diabetes Mellitus	≤ 5	39	32	07	29	10
	6-10	30	19	11	18	12
	11-15	19	09	10	8	11
	16-20	12	01	11	-	12
BMI (Kg/m^2)	<25	78	51	27	48	30
	>25	22	09	13	07	15
HbA1c (%)	<6.5	22	16	06	16	06
	6.5-7	22	18	04	18	04
	7.1-7.5	16	11	05	09	07
	>7.5	40	16	24	12	28

Table-2: Correlation of microalbuminuria and retinopathy with various parameters

	Microalbuminuria +	Microalbuminuria -
Retinopathy +	32	13
Retinopathy -	07	48

Table-3: Correlation between microalbuminuria and retinopathy

(Table-2). The correlation between microalbuminuria and diabetic retinopathy was statistically significant with p value <0.001 (Table-3).

DISCUSSION

Diabetes mellitus is one of the most common metabolic diseases which is either due to the lack of hormone insulin or increase in the insulin resistance. Microvascular complications of diabetes mellitus, especially retinopathy and nephropathy are the leading causes of blindness and end stage renal disease respectively in population of both developed and developing countries.[9,10,11] Diabetes mellitus is being increasingly recognized as a disease, which is characterized by dysfunction of the endothelium. Microalbuminuria marks the onset of endothelial dysfunction related to the kidney. The present study was aimed to study the prevalence as well as correlation of microalbuminuria and retinopathy in patients of Type 2 Diabetes Mellitus. In the present study the prevalence of microalbuminuria was 39%. Similar observations were made by Dasmahapatra et al[12] and Alzaid et al[13] who observed microalbuminuria in 31% and 36% of their study population respectively. Abdelghaffar W et al[9] in their Egyptian study found the prevalence to be 30.7%. However various other studies have recorded the prevalence to be between 16% to 54%. This variation in rates could be a result of the different methods used in those studies, the population and or the ethnic group involved, or variations in controlling blood sugar levels. The prevalence of diabetic retinopathy was observed in 45% patients. Our results were consistent with Rani et al[14] and Reddy et al[15] who observed prevalence of retinopathy in 31% and 36.5% of the study population respectively. The incidence of microalbuminuria increases with that of the age of the patients as observed in our study. 35.4%, 60% and 90% of patients had microalbuminuria in the age group 51-60 years, 61-70 years and above 70 years respectively. The increasing age was reported as one of the risk factors for the development of microalbuminuria in studies conducted by Vijay et al[16], Klein R et al[11] in the Wisconsin study and Nelson et al[17] in Pima Indians. In the present study, it was been observed that longer the duration of diabetes the higher was the prevalence of microalbuminuria and retinopathy. In patients with diabetes for ≤ 5years duration, 17.94% had microalbuminuria and 25.6% had retinopathy whereas, in patients with diabetes for more than 15 years, 91.6% had microalbuminuria and 100% had retinopathy. Varghese et al[18] reported 30.4% microalbuminuria in patients with duration of diabetes less than 5 years whereas 96% patients had microalbuminuria with duration more than 15 years. Huraib et al[19], Nelson et al[17], Chowta et al[20] and Maiti et al[21] showed significant correlation of duration of diabetes with microalbuminuria. Of the 22 patients with BMI of more than 25kg/m^2, 13 had microalbuminuria (59.09%), whereas 15 patients (68.18%) had retinopathy. Similar findings have been brought forth by Patel et al[22] and Jadhav et al[23] who reported that patients with higher body mass index had higher albuminuria. In our study, only 10 out of 44 patients (22.7%) who had HbA1c level up to 7.0% manifested microalbuminuria and retinopathy, whereas, with HbA1c values more than 7.0%, 29 out of 56 patients (51.78%) had microalbuminuria and 35 patients (62.5%) showed evidence of retinopathy. Therefore, even small increments of HbA1c more than 7.0% almost doubles the incidence of microalbuminuria and retinopathy. Poor glycemic control as a risk factor for microalbuminuria was reported in various studies including UKPDS[24], ADVANCE[25] and Herrera

Pombo et al.[26] Our study reported that in addition to HbA1c, BMI and the duration of illness, microalbuminuria has a positive correlation with retinopathy as 32 (82.05%) out of 39 patients with microalbuminuria had retinopathy. Estacio et al[27] also found a positive correlation between albuminuria and retinopathy in 815 patients with type 2 diabetes. The strength of our study is that no such data from the rural population of a tertiary care institute is available till date. Patients of all ethnic groups, ages and sex were included in the study thus, it would be a true representation of the community. However, the present study had its limitations in the form of a smaller sample size, categorization of the patients according to the severity of retinopathy was not done and MICRAL test was not pre-validated with the gold standards i.e. albumin creatinine ratio in our local setting. Better studies with larger sample size need to be planned both at institutional levels and community level to identify the true correlation between microalbuminuria and diabetic retinopathy.

CONCLUSION

The study showed high degree of correlation between microalbuminuria and retinopathy. Most patients, who were positive for microalbuminuria, also had retinopathy. Microalbuminuria may hence be considered as a marker of diabetic retinopathy. Subjects with microalbuminuria are more likely to have diabetic retinopathy than those without albuminuria. Early detection of microalbuminuria and therapeutic intervention (Angiotensin Converting Enzyme inhibitors, Angiotensin Receptor Blockers) in diabetics is vital in preventing the development or slowing the progression of chronic vascular complications. Poor glycemic control, increasing age, duration of diabetes and high BMI are significantly associated with higher incidence of microalbuminuria. Hence, we recommend a closer monitoring of both fundus and microalbuminuria especially in these groups of patients.

REFERENCES

1. Anjana RM, Pradeepa R, Deepa M, Datta M, Sudha V, Unnikrishnan R et al; ICMR-INDIAB Collaborative Study Group. Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerence) in urban and rural India: phase 1 results of Indian Council of Medical Research-INdia DIABetes (ICMR-INDIAB) study. Diabetologia 2011;54:3022-7.
2. Ramachandran A, Snehalatha C, Ma RC. Diabetes in South-East Asia: an update. Diabetes Res Clin Pract. 2014;103:231-7.
3. Taylor R, Williams R. Screening for Diabetic Retinopathy: An overview. Diabetic Medicine. 1994;13:946-52.
4. Parving HH, Gall MA, Skott P, Jorgensen HE, Lokkegaard H, Jorgensen F et al. Prevalence and causes of albuminuria in non-insulin-dependent diabetic patients. Kidney Int. 1992;41:758–62.
5. Standards of Medical Care in Diabetes--2019. Diabetes Care 2019;42:S13-28.
6. Jensen JE, Nielsen SH, Foged L, Holmegaard SN, Magid E. The MICRAL test for diabetic microalbuminuria: predictive values as a function of prevalence. Scand J Clin Lab Invest. 1996;56:117-22.
7. Marshall SM, Shearing PA, Alberti KG. Micral-test strips evaluated for screening for albuminuria. Clin Chem 1992;38:588-91.
8. Phillipou G. Micral-Test. A new semiquantitative test for urinary albumin. Diabetes Care. 1993;16:659-60.
9. Abdelghaffar W, Ghobashy W, Abdo M, El-Baz A, Ibrahim M. Albuminuria as a biomarker for risk of retinopathy in type II diabetic patients in Suez Canal area. Egypt Retina J 2013;1:18-22.
10. Skyler JS. Microvascular complications. Retinopathy and nephropathy. Endocrinol Metab Clin North Am. 2001;30:833-56.
11. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy. III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. Arch Ophthalmol. 1984;102:527-32.
12. Dasmahapatra A, Bale A, Raghuwanshi MP, Reddy A, Byrne W. Incipient and overt diabetic nephropathy in African-American with NIDDM. Diabetes Care 1994;17:297-304.
13. Alzaid AA. Microalbuminuria in patients with NIDDM: an overview. Diabetes Care 1996;19:79-89.
14. Rani Pk, Raman R, Gupta A, Pal SS, KulothunganV, Sharma T. Albuminuria and Diabetic Retinopathy in Type 2 Diabetes Mellitus Sankara Nethralaya Diabetic Retinopathy Epidemiology And Molecular Genetic Study. Diabetol Metab Syndr 2011;3:9.
15. Reddy SC, Kihn YM, Nurjahan MI, Ramil A. Retinopathy in type 2 diabetic patients with microalbuminuria. Nepal J Ophthalmol. 2013;5:69-74.
16. Vijay V, Snehalatha C, Ramachandran A, Viswanathan M. Prevalence of proteinuria in non-insulin dependent diabetes. J Assoc Physicians India. 1994;42:792–4.
17. Nelson RG, Morgenstern H, Bennett PH. An epidemic of proteinuria in Pima Indians with type 2 diabetes mellitus. Kidney Int. 1998;54:2081-8.
18. Varghese A, Deepa R, Rema M, Mohan V. Prevalence of microalbuminuria in type 2 diabetes mellitus at a diabetes centre in southern India. Postgrad Med J. 2001;77:399–402.
19. Huraib S, Abu-Aisha H, Sulimani RA, Famuyiwa FO, Al-Wakeel J, Askar A et al. The pattern of diabetic nephropathy among Saudi Arabia patients with NIDDM. Ann Saudi Med 1995;15:120-124.
20. Chowta NK, Pant P, Chowta MN. Microalbuminuria in diabetes mellitus: Association with age, sex, weight, and creatinine clearance. Indian Journal of Nephrology. 2009;19:53-6.
21. Maiti A, Raychaudhuri P, De J, Mukhopadhaya S, Dey SK, Sinha PK, et al. Changes in Microalbuminuria in Relation to Glycosylated Haemoglobin (HbA1c) and Duration in Type 2 Diabetes Mellitus. Indian Med Gazette. 2012;394-9.
22. Patel KL, Mhetras SB, Varthakavi PK, Merchant PC, Nihalani KD. Microalbuminuria in non-insulin dependent diabetes mellitus. JAPI. 1999;47:596-601.
23. Jadhav UM, Kadam NN. Association of microalbuminuria with carotid Intima-Media thickness

and coronary artery disease- A cross sectional study in Western India. JAPI. 2002;50:1124-1129.

24. UK Prospective Diabetes Study (UKPDS) group. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications with patients of type 2 diabetes (UKPDS 33). Lancet. 1998;352:837-853.
25. The Advance Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Eng J Med. 2008; 358:2560-2572.
26. Herrera-Pombo JL, Aguilar-Diosdado M, Hawkins F, Campos MM, Moreno A, Garcia-Hernandez A et al. Is increasing urinary albumin a better marker for microvascular than for macrovascular complication of type 2 diabetes mellitus? Nephron Clin Prac. 2005;101:116-21.
27. Estacio RO, McFarling E, Biggerstaff S, Jeffers BW, Johnson D, Schrier RW. Overt albuminuria predicts diabetic retinopathy in Hispanics with NIDDM. Am J Kidney Dis. 1998;31:947-53.

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