DOI: 10.14260/jemds/2015/876

ORIGINAL ARTICLE

ALBUMINURIA AND DIABETES MELLITUS TYPE 2: AN OBSERVATIONAL STUDY FROM BARABANKI, LUCKNOW

Vivek Sinha[1], Kashif Shahnawaz[2]

HOW TO CITE THIS ARTICLE:
Vivek Sinha, Kashif Shahnawaz. "Albuminuria and Diabetes Mellitus Type 2: An Observational Study from Barabanki, Lucknow". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 35, April 30; Page: 6008-6016, DOI: 10.14260/jemds/2015/876

ABSTRACT: INTRODUCTION: India leads the world with largest number of diabetic subjects and this is expected to further rise in coming years. Diabetic nephropathy affects 20-30% of patients with diabetes. It presents in its earliest stage with low levels of albumin in the urine (micro-albuminuria). The determination of micro-albuminuria in diabetes mellitus is important as it is the earliest indication of diabetic nephropathy. When left untreated, it will eventually lead to end stage renal disease (ESRD). **OBJECTIVE:** To detect the onset of albuminuria among diabetic patients and the effect of hyperglycemia in causing this condition at an early stage. **MATERIALS AND METHODS:** One hundred clinically diagnosed cases of non-insulin dependent diabetes mellitus (NIDDM) were selected for the study, from Feb-2014 to May-2014 (4 months). Criteria for the diagnosis of DM were of patients having fasting blood glucose levels more than 126 mg/dl. Micro-albuminuria is defined when urinary albumin excretion rate (UAER) in 24-hr urine or short time collected urine during the day time is in the range of 30-300 mg/24-hrs. If excretion is less than 20 µgm/min, the patient is considered to have normo-albuminuria, and if excretion is higher than 200 µgm/min, he is considered to have macro-albuminuria or clinical proteinuria. The data for biochemical analysis are expressed as means±S.E.M. **OBSERVATION:** In our study 35% of the total patients developed albuminuria, while 65% were free from it. 10% patients developed micro-albuminuria who was less than 50 yrs, while it was seen in 15% patients having age more than 50 yrs. Our study shows that only 5% patients developed macro-albuminuria. Glycosylated haemoglobin and fasting plasma glucose was significantly raised among all these patients. Conclusion: Considering the tremendous increase in the number of diabetic patients in India and health budgets of our country, an early detection and good control of diabetes to reduce the burden of diabetic kidney disease is necessary.
KEYWORDS: Albuminuria, Diabetes Mellitus, Nephropathy.

INTRODUCTION: Diabetes mellitus is a disorder of metabolism of carbohydrates, proteins and fats, associated with an absolute and relative insufficiency of insulin secretion accompanied by various degree of insulin resistance. Diabetes mellitus is not a single disease, but a syndrome (Fajans, et al).[1] It is of two types, type-1 & type-2. Type-2 diabetes mellitus is a multifactorial disease that shows heterogenicity in many respects. The prevalence of diabetes mellitus is rapidly rising all over the globe at an alarming rate (Huizinga MM, et al).[2] Recent statistics from the World Health Organisation (WHO) project an increase in the prevalence of diabetes worldwide, particularly in developing countries.[3] Currently India leads the world with the largest number of diabetic subjects and this is expected to further rise in the coming years.[4] The primary driver of the epidemic of the diabetes is the rapid epidemiological transition associated with changes in dietary pattern and decreased physical activities as evident from the higher prevalence of diabetes in the urban population (Mohan V, et al).[5]

DOI: 10.14260/jemds/2015/876

Upto 30% of people with newly diagnosed Type-2 diabetes will already have abnormally high urine albumin levels; about 75% of these people will have micro-albuminuria and about 25% will have overt diabetic nephropathy (Delcourt C, et al,[6] & Krolewski A S, et al.[7]) Diabetic nephropathy, or diabetic kidney disease, affects 20 to 30 percent of patients with diabetes. It is a common cause of kidney failure. The proportion of patients with end stage renal disease (ESRD) caused by diabetes has progressively increased during the last few decades and diabetic nephropathy is now the single most common cause of ESRD in worldwide.[8] Diabetic nephropathy presents in its earliest stage with low levels of albumin (micro-albuminuria) in the urine (Gall M A, et al).[9] Diabetic nephropathy is typically defined by macro-albuminuria, i. e., a urinary albumin excretion of more than 300mg in a 24hr collection- or macroalbuminuria and abnormal renal function as represented by an abnormality in serum creatinine, calculated creatinine clearance, or glomerular filtration rate (GFR). Clinically, diabetic nephropathy is characterized by a progressive increase in proteinuria and decline in GFR, hypertension, and a high risk of cardiovascular morbidity and mortality. In diabetic patients with proteinuria the relative mortality is about 40 times higher than in diabetics without proteinuria. It is estimated that death due to renal disease is 17 times more in diabetics than in non-diabetics. It is now established that in both type-I & type-II DM, urinary excretion of small amounts of albumin (microalbuminuria) is predictive of morbidity and mortality due to renal complications and cardio-vascular disease.[10-12]

Micro-albuminuria is now recognized as an independent risk factor, even in the absence of diabetes. The determination of micro-albuminuria in diabetes mellitus is important as it is the earliest indication of diabetic nephropathy which if left untreated, will eventually lead to end stage renal disease. Micro-albuminuria is best determined on a 24hr urine sample. For convenience a random sample can also be used and the test done with the Micral Test Strip (Leong S O, et al,[13] & Ng W Y, et al.[14])

Main objective of our present study is to detect the onset of albuminuria among diabetic patients and the effect of hyperglycemia in causing this at an early stage, so that the renal complications can be prevented.

MATERIALS AND METHODS: Present study was carried out in the department of Biochemistry, Mayo Institute of Medical Sciences, Barabanki, Luckhnow, U. P, on the clinically diagnosed cases of diabetes mellitus. The study period was from Feb- 2014 to May- 2014. The patients were either on diet control or taking drugs. These cases were selected from the outdoor and indoor departments. Permission from concerned authorities was duly obtained.

In our study 100 cases of known diabetes mellitus was selected from different age group ranging from 30 to 60 years. Their consent was taken. All the cases in the study group were clinically of non-insulin dependent diabetes mellitus, Type-2 (NIDDM). The diagnosis of diabetes mellitus was made on the basis of history, physical examination and the laboratory investigations of urine & blood. The criteria for the diagnosis of diabetes mellitus were of patients having the fasting blood glucose levels more than 126 mg/dl.

The blood glucose level was estimated by glucose oxidase peroxidise (GOD/POD; Accurex Biomedicals Pvt. Ltd.) and Glycosylated haemoglobin by Ion Exchange Resin Separation Method. The Glycosylated haemoglobin (HbA1c) test was done by test kit, (manufactured by Erba Diagnostics-Mannheim GmbH Germany and marketed by Transasia Pvt. Ltd.) Microalbumin was estimated in all

DOI: 10.14260/jemds/2015/876

samples by the kit supplied by Biosystems S. A. Costa Brava 30, Barcelona, Spain. Serum urea and creatinine were estimated by kit supplied by Span diagnostics. Two ml of blood was withdrawn from the selected site (Antecubital vein) and transferred to EDTA vials for the estimation of HbA1C levels. The blood was mixed properly with the anticoagulant by gentle shaking. For the estimation of blood glucose, 2 ml of blood was withdrawn from the antecubital vein and transferred to sodium fluoride-potassium oxalate vials.

Micro-albuminuria has been defined using different units of measurements. According to Gento-Montecatini, micro-albuminuria is present when the urinary albumin excretion rate (UAER) in 24-hour urine or short time collected urine during daytime is in the range of 30-300 mg/24hr (20-200 microgm/min), which is equivalent to 0.46 to 4.6 micromol/24 hr. Urine sample should be collected when the patient is at rest and his diabetes is under average clinical control. No measurement should be made in patients with ketosis or poor control until proper control is established. If excretion is lower than 20 microgm/min, the patient is considered to have normo-albuminuria, and if excretion is higher than 200 microgm/min, he is considered to have macro-albuminuria or clinical proteinuria. Micro-albuminuria should be present in at least two of three urine samples collected over a period of several months.[9,10] The data for biochemical analysis are expressed as mean±S. E. M. The entire data was analyzed by using the statistical package program SPSS.

OBSERVATIONS:

Type of patients studied	Percentage
Patients with albuminuria	35
Patients without albuminuria	65

Table 1: Diabetic Patients with or without albuminuria

Above table shows that, 35% of the total patient developed albuminuria and 65% patients were free from any type of albuminuria.

Age of patients (in Yrs)	Number of patients with micro-albuminuria	Number of patients with frank proteinuria
Less than 50 years	10	5
More than 50 years	15	5

Table 2: Age-wise distribution of diabetic patients with micro-albuminuria & frank proteinuria

DOI: 10.14260/jemds/2015/876

Serial No.	Age (in Yrs)	Micro-albuminuria (in mg/day)	Fasting plasma glucose (in mg/dl)	HbA1C (in %)
1	31	48	159	9.3
2	39	105	152	7.8
3	45	250	198	9.6
4	49	72	146	7.9
5	32	290	129	9.8
6	38	85	130	9.8
7	47	52	203	8.6
8	35	170	196	9.3
9	36	86	160	8.7
10	41	156	165	9.3
Mean±S.E.M		**131±26.46**	**163±8.55**	**9.01±0.23**

Table 3: Level of micro-albuminuria, fasting plasma glucose and HbA1C among diabetic persons less than 50 years of age

The data present in the above table shows that, micro-albuminuria was directly correlated with fasting plasma glucose and HbA1C among the person who is less than 50 yrs of age. There is an increase in urinary micro-albumin with the increase in HbA1C and fasting plasma glucose. It also appears that the total number of patients with micro-albuminuria were only 10 out of 100. That indicates only 10% patient developed micro-albuminuria who was less than 50 yrs.

Serial No.	Age (in Yrs)	Fasting plasma glucose (in mg/dl)	Micro-albuminuria (in mg/day)	HbA1C (in %)
1	72	172	187	7.7
2	58	132	232	10.5
3	51	195	280	8.2
4	58	132	232	10.5
5	62	220	234	7.9
6	67	129	52	8.9
7	81	165	79	8.8
8	70	182	96	7.8
9	71	156	272	8.0
10	62	220	256	8.2
11	60	198	108	8.0
12	77	152	208	9.2
13	60	145	48	8.1
14	75	139	170	9.6
15	78	160	92	9.2
Mean±S.E.M		**166.46±7.91**	**169.73±21.37**	**8.706±24**

Table 4: Level of fasting plasma glucose, micro-albuminuria, & HbA1C among diabetic persons more than 50 years of age

The data available in the above table shows that, there is an increase in urinary micro-albumin with the increase in HbA1C and fasting plasma glucose in the patients of more than 50 yrs of age. It also appears that the total number of patients with micro-albuminuria were only 15 out of 100. That indicates only 15% patient developed micro-albuminuria who were more than 50 yrs of age.

DOI: 10.14260/jemds/2015/876

Serial No.	Age in Years	Micro-albuminuria (in mg/day)	Serum Urea (in mg/dl)	Serum Creatinine (in mg/dl)
1	31	48	35	0.9
2	39	105	34	1.1
3	45	250	22	1.2
4	49	72	35	0.8
5	32	290	33	1.3
6	38	85	20	0.7
7	47	52	24	0.7
8	35	170	38	0.8
9	36	86	38	0.4
10	41	156	40	0.9
Mean±S.E.M		**131.40±26.46**	**31.90±2.27**	**0.88±0.084**

Table 5: Level of micro-albuminuria, Serum urea & creatinine among diabetic persons less than 50 years of age

Above table shows that the group of patients below 50 yrs of age who developed micro-albuminuria (131.40±26.46) did not had increased levels of serum urea & creatinine. Their urea and creatinine levels were in normal range.

Serial No.	Age in Yrs	Micro-albuminuria (in mg/day)	Serum Urea (in mg/dl)	Serum Creatinine (in mg/dl)
1	72	187	28	0.7
2	58	232	29	0.8
3	51	280	34	0.9
4	58	232	29	0.8
5	62	234	22	0.9
6	67	52	24	0.9
7	81	79	30	1.1
8	70	96	40	1.2
9	71	272	24	0.9
10	62	256	23	0.9
11	60	108	39	1.0
12	77	208	32	0.8
13	60	48	32	1.1
14	75	170	30	0.8
15	78	92	24	1.2
Mean±S.E.M		**169.73±21.37**	**29.3±1.42**	**0.93±0.039**

Table 6: Level of micro-albuminuria, Serum urea & creatinine among diabetic persons more than 50 years of age

DOI: 10.14260/jemds/2015/876

Above table shows that the group of patients above 50 years of age who developed micro-albuminuria (169.73±21.37) did not had increased serum urea & creatinine levels. Their serum urea and creatinine levels were in normal range.

Serial No.	Age in yrs	Total Urinary Protein (in mg/day)	HbA1C (in %)	Fasting plasma glucose (in mg/dl)
1	50	1200	11.0	165
2	48	3200	13.2	136
3	39	2900	10.2	152
4	43	2600	12.8	194
5	42	2200	11.2	178
Mean±S.E.M		2420±346.98	11.68±56	165±10.04

Table 7: Level of frank proteinuria, HbA1C, and plasma fasting glucose among diabetic persons less than 50 years of age

Above table shows that only 5% of patients developed macro-albuminuria. Glycosylated haemoglobin as well as fasting plasma glucose was significantly raised among all these patients. All these patients belonged to less than 50 years of age group.

Serial No.	Age in yrs	Total Urinary Protein (in mg/day)	HbA1C (in %)	Fasting plasma glucose (in mg/dl)
1	70	2740	11.1	172
2	60	2400	9.8	192
3	69	1560	9.3	210
4	52	2580	12.6	155
5	52	3300	12.2	178
Mean±S.E.M		2516±285	11.0±0.64	181.40±9.29

Table 8: Level of macro-albuminuria, HbA1C, & fasting plasma glucose among diabetic persons more than 50 years old

Above table shows that only 5% of the patients developed macro-albuminuria. Glycosylated haemoglobin as well as fasting plasma glucose was significantly increased among all these patients. All these patients belong to more than 50 years of age group.

DISCUSSION: In this study, it was observed that, 35% of total patients developed albuminuria and 65% patients were free from any type of albuminuria. Also, micro-albuminuria was present in 10% of the patients less than 50 yrs of age, while 15% of the patients more than 50 yrs of age were having micro-albuminuria. Various epidemiological and cross sectional studies have reported marked variation in the prevalence of micro-albuminuria.[15-18] Gupta et al reported a prevalence of 26.6% in 65 type-2 north Indian non-proteinuric patients,[19] while John et al reported a prevalence of 19.7% from a tertiary hospital in Vellore, south India.[20] Vijay et al,[21] reported that 15.7% had proteinuria among 600 type-2 diabetic patients studied at a diabetic centre in Channai city.[21]

DOI: 10.14260/jemds/2015/876

The variation in the prevalence can be attributed to factors such as differences in populations, in the definitions of micro-albuminuria, method of urine collection, etc.

Our study also shows that there is an association between albuminuria and age of the patients, level of HbA1C, and levels of serum urea and creatinine. Gupta et al,[19] reported HbA1C to be associated with micro-albuminuria. John et al,[20] reported male sex, older age, longer duration of diabetes, poor glycemic control, and raised blood pressure as risk factors of micro-albuminuria, while Vijay et al,[21] reported duration of diabetes, systolic and diastolic blood pressure, age of the patients, and serum creatinine to be associated with proteinuria. Age was reported as one of the risk factors in the Wisconsin Study,[17] in a Danish population study,[22] and in Pima Indians.[23] The association of glycemic control with micro-albuminuria has been well established by various studies.[17,22-24]

Early stage of diabetic nephropathy (DN) is characterized by a small increase in urinary albumin excretion (UAE), also called micro-albuminuria or incipient DN (Mogensen CE & Christensen CK).[11] More advanced disease is defined by the presence of macro-albuminuria or proteinuria. The latter is classically named overt DN. More recent studies suggest that only 30 to 45% of micro-albuminuric patients will progress to proteinuria over 10 yrs of follow-up (Gross J L, et al).[25]

Hyperglycemia is a significant risk factor for the development of microalbuminuria in diabetes mellitus (Ravid M et al).[26] A reduction of 1% in HbA1C is associated with 37% decrease in microvascular endpoints. Proteinuria itself could lead to progression of DN. Proteinuria of more than 2gm/24hr is associated with a greater risk of ESRD (Ruggenenti P, et al,[27] & Remuzzi G, et al.[28])

CONCLUSION: It was observed in our study that the normal subjects, in which the blood sugar (F & PP) and HbA1C was in normal range, microalbuminuria was not observed significantly. There was an increase in microalbumin with the increase in HbA1C and fasting plasma glucose. It was also observed that the highest number of person with having micro-albumin belonged to more than 50 years of age group. Given the high prevalence of diabetes in Indians with over 20 million diabetes already and the numbers expected to increase to 57 million diabetics by the year 2025, this could place considerable burden on the health budgets of this country. This calls for early detection and good control of diabetes to reduce the burden of diabetic kidney disease in the future.

REFERENCES:

1. Fajans S S, Cloutier M C, Crowther R L. The Banting Memorial Lecture 1978. Clinical and etiologic heterogenicity of idiopathic diabetes mellitus. Diabetes 1978; 27: 1112-1125.
2. Huizinga M M, Rothman R L. Addressing the diabetes pandemic: A comprehensive approach. Indian J Med Res 2006; 124: 481-484.
3. King H, Auberti R E, Herman W H. Global burden of diabetes, 1995-2025. Prevalence, numerical estimated and projections. Diabetes Care 1998; 2: 1414-31.
4. Ramachandran A, Snehalatha C, Latha E, et al. Rising prevalence of NIDDM in an urban population in India. Diabetolgia 1997; 40: 232-7.
5. Mohan V, Sandeep S, Deepa R, Shah B, & Varghese C. Epidemiology of type-2 diabetes: Indian Scenario. The Indian J Med Res 2007; 125 (3): 217-230.
6. Delcourt C, Vauzelle-Kervroedan F, Cathelineau G, Papoz L. Low prevalence of long term complications in non-insulin dependent diabetes mellitus in France: A multicentre study. Journal of Diabetes and its Complications. Mar-Apr 1998; 12 (2): 88-95.

7. Krolewski A S, Laffel L M B, Krolewski M, Quinn M, Warram J H; Glycosylated haemoglobin and the risk of micro-albuminuria in patients with insulin dependent diabetes mellitus. N Eng J Med 1995; 332: 1251-55.
8. Cordonnier D, Bayle F, Benhamou P Y, et al. Future trnds of management of renal failure in diabetes. Kidney Int 1993; 43: 8-13.
9. Gall M A, Neilsen F S, Schmidt U M and Parving H H. The course of kidney function in type-2 (non-insulin dependent) diabetic patients with diabetic nephropathy. Diabetolgia 1993; 36: 1071-1078.
10. Alberti KGMM. Problems related to definitions and epidemiology of type-II DM. Diabetolgia 1993; 36: 948-984.
11. Mogensen C E, Chachati A, Christensen C K, et al. Micro-albuminuria: an early marker of renal involvement in diabetes. Uremia Invest 1985-1986; 9: 85-96.
12. Mogensen C E. Micro-albuminuria as predictor of clinical diabetic nephropathy. Kidney Int 1987; 3: 673-689.
13. Leong S O, Lui K F, Ng W Y, Thai A C. The use of semiquantitative urine test strip (Micral) for micro-albuminuria screening in patients with diabetes mellitus. Singapore Med Jour 1998; 39 (3): 101-3.
14. Ng W Y, Lui K F, Thai A C. Evaluation of a rapid screening test for micro-albuminuria with a spot measurement of urine albumin-creatinine ratio. Ann Acad Med Singapore 2000; 29: 62-5.
15. Mogensen C E, Neldam S, Tikkanen I, Oren S, Viskoper R, Watts R W, Cooper M E. Randomised controlled trial of dual blockage of renin-angiotensin system in patients with hypertension, micro-albuminuria and non-insulin dependent diabetes. The candesartan and lisinopril micro-albuminuria (CALM) Study. B M J 2000; 321 (7274): 1440-44.
16. Christensen P K, Gall M A, Parving H H. Course of glomerular filtration rate in albuminuric type-2 diabetic patients with or without diabetic glomerulopathy. Diabetes Care 2000; 23 (Suppl. 2): B14-B20.
17. Klein R, Klein B E K, Moss S E. Prevalence of micro-albuminuria in older onset diabetes. Diabetes Care 1993; 16: 1325-9.
18. Allawi J, Rao P V, Gilbert R, et al. Micro-albuminuria in non-insulin dependent diabetes: its prevalence in Indian compared with Europid patients. BMJ 1988; 296: 462-4.
19. Gupta D K, Verma L K, Khosla P K, et al. The prevalence of micro-albuminuria in diabetes: a study from north India. Diabetes Res Clin Pract 1991; 12: 125-8.
20. John L, Rao P S, Kanagasabapathy A S. Prevalence of diabetic nephropathy in non-insulin dependent diabetes. Ind Jour Med Res 1991; 94: 24-9.
21. Vijay V, Snehalatha C, Ramachandran A, et al. Prevalence of proteinuria in non-insulin dependent diabetes. J Assoc Physicians India 1994; 42: 792-4.
22. Schmitz A, Vaeth M. Micro-albuminuria: a major risk factor in non-insulin dependent diabetes: a 1-yr follow-up study of 503 patients. Diabet Med 1987; 5: 126-34.
23. Nelson R G, Kunzelman C L, Pettit D J, et al. Albuminuria in type-2 (non-insulin dependent) diabetes mellitus and impaired glucose tolerance in Pima Indians. Diabetolgia 1989; 32: 870-6.
24. Haffner S M, Morales P A, Gruber M K, et al. Cardiovascular risk factors in non-insulin dependent diabetes subjects with micro-albuminuria. Arterioscler Thromb 1993; 13: 205-10.

DOI: 10.14260/jemds/2015/876

25. Gross J L, de Azevedo M J, Silveiro S P, Canani L H, Caramori M L, Zelmanovitz T. Diabetic Nephropathy: diagnosis, prevention and treatment. Diabetes Care 2005; Jan 28 (1): 164-76.
26. Ravid M, Lang R, Rachmani R, Lishner M. Long term renoprotective effect of angiotensin converting enzyme inhibition in non-insulin dependent diabetes mellitus. A 7-year follow-up study. Arch Intern Med 1996; Feb 12, 156 (3): 286-9.
27. Ruggenenti P, Gambara V, Perna A, Bertani T, Remuzzi G. The nephropathy of non-insulin dependent diabetes: predictors of outcome relative to diverse patterns of renal injury. J Am Soc Nephrol 1998; 9 (12): 2336-43.
28. Remuzzi G, Bertani T. Is glomerulosclerosis a consequence of altered glomerular permeability to macromolecules? Kidney Int 1990; 38: 384-94.

AUTHORS:

1. Vivek Sinha
2. Kashif Shahnawaz

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Biochemistry, Mayo Institute of Medical Sciences, Barabanki, Luckhnow, UP.
2. Assistant Professor, Department of Community Medicine, MGM Medical College & LSK Hospital, Kishanganj, Bihar.

FINANCIAL OR OTHER COMPETING INTERESTS: None

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Kashif Shahnawaz,
Manhar Road,
Chhoti Quazipura,
District Darbhanga-846004,
Bihar.
E-mail: kashif.shahnawaz98@gmail.com

Date of Submission: 14/04/2015.
Date of Peer Review: 15/04/2015.
Date of Acceptance: 22/04/2015.
Date of Publishing: 28/04/2015.