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Association of Cardiovascular Disease with Micro Albuminuria in Type 2 Diabetes Mellitus - Study in A Tertiary Care Hospital

Md Jahirul Haque[1], Md. Nazrul Islam[2], Md. Zakaria Al Aziz[3], Shah Mohammad Ashrafuzzaman[4], Gobindo Chandra Banik[5], AKM Sajedur Rahman[6], Sarmistha Biswas[7], HAM Nazmul Ahasan[8]

Abstract

Introduction: *Microalbuminuria appears to be the earliest sign and predictor of the subsequent diabetic renal disease and is a marker of increased cardiovascular morbidity and mortality. It is also a predictor of morbidity and mortality in patients who do not have evidence of significant renal disease.*

Objective: *To evaluate the association of microalbuminuria in type 2 DM with cardiovascular diseases and to correlate microalbuminuria with age of onset in type 2 diabetes mellitus.*

Materials and Method: *A hospital based observational study was carried out in the Department of Medicine, Dhaka Medical College & Hospital,Dhaka, from January 2014 to November 2014. A total of 100 patients diagnosed as type 2 diabetes mellitus according to American Diabetic Association guideline were included in this study. Association of microalbuminuria with cardiovascular diseases was determined by statistical analysis and regression analysis.*

Results: *The majority (40.0%) of patients were in 5th decade and the mean (±SD) age was 57.17±11.2 years. According to BMI it is observed that majority of patients were obese in both groups, where male 66.0% and female 75.5%.The occurrence of cardiovascular diseases in type 2 diabetes mellitus patients is increasing with duration of DM, where 61.9% found in newly diagnosed DM. It was observed that 38(38.0%) patients had normoalbuminuria (<30 mg/gm), their mean ACR was 17.6±8.1 mg/gm and 62(62.0%) patients had microalbuminuria (30-300 mg/gm), their mean ACR was 158.7±88.3 mg/gm. Microalbuminuria was found 53(67.1%) and 9(42.9%) patients with cardiovascular diseases and without cardiovascular diseases respectively. Occurrence of microalbuminuia was found significantly higher (p<0.05) in type 2 DM patients with cardiovascular diseases.*

Conclusion: Microalbuminuria is found strongly associated with cardiovascular diseases in type 2 diabetes mellitus patients and there is 2.72 times more chance of developing cardiovascular diseases.

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1. Associate Professor (CC),Department of Medicine, Shaheed Syed Nazrul Islam Medical College, Kishoreganj
2. Senior Consultant (Medicine), Narayanganj General Hospital, Narayanganj.
3. Assistant Professor, Department of Medicine, Sheikh Hasina Medical College, Tangail
4. Assistant Professor, Department of Medicine, Mymensingh Medical College, Mymensingh.
5. Associate Professor, Department of Medicine, Dhaka Medical College, Dhaka.
6. Assistant Professor, Department of Medicine, Cumilla Medical College, Cumilla.
7. Associate Professor, Department of Medicine, Dhaka Medical College, Dhaka.
8. Professor of Medicine, Popular Medical College, Dhaka.

Address of Correspondence: Dr. Md. Jahirul Haque, Associate Professor (CC), Medicine, Shaheed Syed Nazrul Islam Medical College, Kishoreganj, Mobile: 01711-884838, E-mail: jahirulhaque69@gmail.com

Introduction:

Diabetes mellitus (DM) is associated with an increased risk for cardiovascular morbidity and mortality and is one of the most common chronic diseases in nearly all countries. Incidence and prevalence of diabetes mellitus and cardiovascular diseases are increasing worldwide. Both developed countries and developing countries are facing this increasing burden of death toll and health expenditure. Microalbuminuria is a diagnostic tool that has shown enormous potentiality in predicting adverse cardiac events in both diabetic and non diabetic patients. Microalbuminuria is defined as excretion of 30–300 mg of albumin per 24 hours (or 20–200 μg/min or 30–300 μg/mg creatinine) on 2 of 3 urine collections over 3-6 months period[1]. Although 24-hour excretion has traditionally been preferred, the albumin/creatinine ratio has been shown to be a similarly

valid screening tool for diabetic nephropathy[2,3]. The detection of low levels of albumin excretion (microalbuminuria) has been linked to the identification of incipient diabetic kidney disease. Microalbuminuria is a predictor of outcome in patients with renal disease. Additionally, it is a predictor of morbidity and mortality in patients who do not have evidence of significant renal disease. In patients with hypertension, microalbuminuria has been correlated to left ventricular hypertrophy. Both in hypertensive and normotensive patients, microalbuminuria predicts an increased risk of cardiovascular morbidity and mortality[4]. Microalbuminuria may be related to cardiovascular damage by several biological pathways. The amount of albumin in the urine is traditionally thought to depend on the electrochemical characteristics of the glomerular membrane barrier, the intraglomerular pressure and tubular reabsorption[5].Microalbuminuria is also associated with the metabolic syndrome, which includes insulin resistance, low HDL cholesterol levels, high triglyceride levels, and truncal obesity[6].Microalbuminuria has been studied extensively as predictor for cardiovascular diseases[7] in Diabetes mellitus and in non diabetic patients. This study was intended to evaluate the association of microalbuminuria with cardiovascular diseases in type 2 DM[8,9] and analyze its potentiality among the study population.

Materials and Methods:

A hospital based observational study was carried out in the Department of Medicine, Dhaka Medical College & Hospital,Dhaka, from January 2014 to November 2014,with an aim to determine the demographic profile, presence of microalbuminuria, frequency of cardiovascular diseases, correlate association of microalbuminuria and cardiovascular diseases and to correlate microalbuminuria with age of onset in type 2 DM. A total of 100 patients diagnosed as type 2 DM according to American Diabetic Association guideline[10] were included in this study.Detailed history including duration of diabetes mellitus, medications received, associated hypertension, any other cardiovascular diseases and its medication, any history suggestive of adverse cardiac events along with prescribed medication was obtained. Presence of hypertension, evidence of diabetic complications, peripheral vascular disease and presence of cardiovascular diseases were evaluated by clinical examination, previous and recent investigation report. Investigation was done to ascertain presence of micro-albuminuria by spot urine sample examination for ACR[2,3] (urinary albumin creatinine ratio) in the department of Biochemistry in Banghabandhu Sheikh Mujib Medical University (BSMMU) by Dimension Clinical Chemistry System (Particle-enhanced Turbidimetic Inhibition Immunoassay Method). Subjects were classified according to the ACR[2,3]: <30 mg/gm creatinine as normoalbuminuric, 30-300 mg/gm creatinine as microalbuminuric and >300 mg/gm creatinine as macroalbuminuric. Fasting plasma glucose (FPG) and plasma glucose 2-h postload, HbA_{1c} and other relevant investigations were done in the department of Pathology and Biochemistry, Dhaka Medical College. Presence of cardiovascular diseases was determined by fasting lipid profile, X-ray chest P/A view and CT scan of brain ECG and Echocardiogram. Echocardiogram was done 2D, M Mode and Colour Doppler by expert cardiologist. Association of microalbuminuria with cardiovascular diseases was determined by statistical analysis and regression analysis.

Results:

Table I. *Distribution of the study population by age with sex (n=100)*

Age (in year)	Male	Female	No. of patients (n=100)	Percentage
≤50	12	28	40	40.0%
51-60	13	11	24	24.0%
61-70	14	10	24	24.0%
71-80	8	3	11	11.0%
>80	0	1	1	1.0%
Total	47	53	100	100%

Table I shows that majority (40.0%) patients belonged to age ≤50 years.

Table II

Distribution of the study population by BMI (n=100)

BMI (kg/m^2)	Number of Patients	Percentage
Normal (<23)	9	9.0
Over weight (23-24.9)	20	20.0
Obese (≥25)	71	71.0

Table II shows that majority of patients were obese.

Table III

Distribution of the study population by duration of DM with cardiovascular disease (n=100)

Duration of DM (years)	Total number of patients	Cardiovascular diseases				95% CILower, Upper
		Present(n=79)		Absent(n=21)		
Newly detected	21	13	61.9%	8	38.1%	41.1, 82.7
0-5	42	31	73.8%	11	26.2%	60.5, 87.1
6-10	19	17	89.5%	2	10.5%	74.9, 99.9
>10	18	18	100%	0	0.0%	-

Table III shows that occurrence of cardiovascular diseases in type 2 diabetes mellitus patients is increasing with duration of DM.

Table IV

Distribution of the study population by cardiovascular diseases with clinical variables (n=79)

Cardiovascular diseases	Total (n=79)	Percentage
HTN	21	26.6
IHD	4	5.1
Stroke	4	5.1
HTN+IHD	17	21.5
HTN+Stroke	17	21.5
IHD+Stroke	3	3.8
HTN+IHD+Stroke	13	16.5

Table IV shows that 79 patients had cardiovascular diseases.

Table Va. Distribution of the study population by spot urine ACR (n=100)

Spot urine ACR (mg/gm)	Male	Female	Total patients (n=100)	Percentage	Mean±SD	95% CILower, Upper
30-300 (Microalbuminuria)	33	29	62	62.0%	158.7±88.3	52.5, 71.5
<30 (Normoalbuminuria)	14	24	38	38.0%	17.6±8.1	28.5, 47.5
Total	47	53	100	100.0%	105.04±97.8	

Table Va shows that 62(62.0%) patients had microalbuminuria (30-300 mg/gm) and their mean ACR was 158.7±88.3 mg/gm. And 38(38.0%) patients had normoalbuminuria (<30 mg/gm), their mean ACR was 17.6±8.1 mg/gm.

Table Vb: *Distribution of the study population by HbA1c (n=100)*

HbA1c (%)	Male	Female	Total patients(n=100)	Percentage	Mean±SD	95% CILower, upper
≤6.5	5	11	16	16.0%	6.0±0.5	8.8, 23.2
>6.5	42	42	84	84.0%	9.1±2.3	76.8, 91.2
Total	47	53	100	100.0%	8.63±2.4	

Table Vb shows that majority (84.0%) patients had >6.5 HbA1c.

Table Vc: Distribution of the study populationshowing relation between HbA1cand cardiovascular diseases (n=100)

Cardiovascular diseases	HbA1c (%)	Male	Female	Total	Percentage	P value
Present (n=79)	≤6.5	4	8	12	12.0	0.266^{ns}
	>6.5	34	33	67	67.0	
Absent (n=21)	≤6.5	1	3	4	4.0	0.413^{ns}
	>6.5	8	9	17	17.0	
Total		47	53	100	100.0	

Table Vc shows that there is no significant difference between male and female patients with or without cardiovascular diseases and HbA1c level.

TableVd: *Relation of microalbuminuria withHbA$_{1c}$ (n=100).*

Spot Urine ACR (mg/gm)	HbA1c %				P value
	≤6.5%(n=16)		>6.5%(n=84)		
	n	%	n	%	
30-300 (microalbuminuria)	3	18.8	59	70.2	0.001^{s}
<30 (normoalbuminuria)	13	81.2	25	29.8	

Table Vd shows that presence of microalbuminuria in study population is gradually increasing in uncontrol (HbA1c>6.5%) diabetes mellitus patients.

Table VI: Correlation ofmicroalbuminuria with duration of type 2 diabetes mellitus patients (n=100).

Duration of DM (years)	Total Number	Spot urine ACR (mg/gm)				95% CILower, Upper
		Normoalbuminuria (n=38)		Microalbminuria (n=62)		
Newly detected	21	10	47.6%	11	52.4%	31.0, 73.8
0-5	42	19	45.2%	23	54.8%	39.7, 69.9
6-10	19	6	31.6%	13	68.4%	47.5, 89.3
>10	18	3	16.7%	15	83.3%	66.7, 99.9

Table VI shows that presence of microalbuminuria in study population is gradually increasing along with duration of DM and it was high in > 10 years duration of DM group (83.3%).

Table VII

Relation of microalbuminuria in between cardiovascular diseases and without cardiovascular diseases in patients having type 2 diabetes mellitus(n=100).

Urine spot ACR (mg/gm)	Cardiovascular diseases				OR	95% CILower, upper	P value
	Present(n=79)		Absent(=21)				
	N	%	n	%			
30-300 (microalbuminuria)	53	67.1	9	42.9	2.72	0.92, 8.15	0.042^{s}
<30 (normoalbuminuria)	26	32.9	12	57.1			

Table VII shows that with cardiovascular disease26(32.9%) patients had normoalbuminuria and 53(67.1%) had microalbuminuria. Without cardiovascular diseases 12(57.1%) had normoalbuminuria and 9(42.9%) had microalbuminuria. Occurrence of microalbuminuia was found significantly higher ($p<0.05$) in type 2 DM patients with cardiovascular diseases.

Discussion:

Majority (40.0%) patients were in 5th decade and the mean (±SD) age was 57.17±11.2 years, ranging from 40 to 85 years. The mean (±SD) age was 60.7±10.1 years and 54.04±11.4 years in male and female respectively and the mean age was significantly (P<0.05) higher in male patients. Similarly, Farshchi et al. (2014)[11] showed the mean (±SD) age of male patients was 55.5±8.1 years and female patients was 51.8±7.6 years, that was also significantly (P<0.05) higher in male patients and another study in Bangladesh[6] by Masum et al. (2012)[12] showed the mean age was 56.5 ± 11.2 years in male patients and 54.3 ± 10.8 years in female patients, which are comparable with this study. Study subjects were categorized as overweight and obese on the basis of the Asia Pacific Classification[13], BMI> 23.0 is overweight and >25.0 is obese. The mean BMI was found 25.9±2.3 kg/m^2. Venugopal and Iyer (2010)[14] reported that majority of their study subjects were overweight or obese and In Alharf (2012)[15] study obtained that both males and females had mean BMI of about 30 kg/m^2, which are consistent with this study. It was observed that the occurrence of cardiovascular diseases in type 2 DM[8,9] patients is increasing with duration of DM, where 61.9% found in newly diagnosed DM, 73.8% in duration of DM 0 – 5 years, 89.5% in duration of DM 6 – 10 years & 100.0% in more than 10 years duration of DM of study population. In this study it was observed that 79 patients had cardiovascular diseases, among them HTN was found in 21(26.6%) patients, IHD was 4(5.1%) patients and stroke was 4(5.1%) patients. Other patients was found in combination of more than one disease. The percent of patients who have hypertension was 38.5% observed by Ibrahim et al. (2012)[16], which support this study. It was observed that 38(38.0%) patients were normoalbuminuric (<30 mg/gm), their mean ACR was 17.6±8.1 mg/gm and 62(62.0%) patients were microalbuminuric (30-300 mg/gm), their mean ACR was 158.7±88.3 mg/gm. The Microalbuminuria Prevalence (MAP) study found a high prevalence of microalbuminuria (39.8 %) in Asian hypertensive type 2 diabetic subjects (Wu et al. 2005)[17]. Majority (84.0%) patients had >6.5 HbA1c. Mean HbA1c was found 8.63±2.4%. Masum et al. (2012)[12] found the mean HbA_{1c} was 8.8 ± 1.4% in male patients and 8.2 ± 1.3% in female patients. Presence of microalbuminuria in study population is gradually increasing in uncontroled (HbA1c >6.5%) diabetes mellitus patients and also increasing along with duration of DM and it was high in >10 years duration of DM group (83.3%). Similarly Prasanna (2011)[18] reported that as the duration of diabetes increases, there is increased incidence of microalbuminuria. In this study 79 patients had cardiovascular diseases, among them 26(32.9%) patients had normoalbuminuria and 53(67.1%) had microalbuminuria. Without cardiovascular diseases was found 21 patients among them 12(57.1%) had normoalbuminuria and 9(42.9%) had microalbuminuria. Occurrence of microalbuminuia was found significantly higher (p<0.05) in type 2 DM[8,9] patients with cardiovascular diseases. MicroAlbuminuria Prevalence (MAP) Wu et al. (2005)[17] study found a high prevalence of microalbuminuria 39.8 % in Asian hypertensive type 2 diabetic[8,9] subjects. In Venugopal and Iyer (2010)[14] study showed the prevalence of microalbuminuria in diabetic subjects with hypertension, was found to be 39.2%.

Conclusion:

Microalbuminuria is an important predictor for development of cardiovascular diseases in type 2 DM. The occurrence of cardiovascular diseases in type 2 DM patients is increased with duration of DM. There is also increased HbA1c in most of the patients. Presence of microalbuminuria is gradually increasing along with duration of DM and specially higher in more than 10 years duration in most of uncontrolled DM. Microalbuminuria is found strongly associated with cardiovascular diseases in type 2 DM patients and there is 2.72 times more chance of developing cardiovascular diseases.

Referrences:

1. Microalbuminuria,Guidelines,LMP,2012: Available from: http://santana0612.files.wordpress.com/2009/09/microalb.pdf.
2. Edgar V Lerma. Proteinuria [Internet]. *Medscape: 2012. Available from: https://emedicine.medscape.com/article/238158-overview#a1*
3. Vecihi Batuman. Diabetic Nephropathy [Internet]. *Medscape: 2011. Available from: https://emedicine.medscape.com/article/238946-overview*
4. Bishnu P Devkota. Microalbumin [Internet]. Medscape: 2014. Available from: https://emedicine.medscape.com/article/2088184-overview
5. Parving HH, Mogensen CE, Jensen HA, Evrin PE, 'Increased urinary albumin-excretion rate in benign essential hypertension', 1974; *Lancet.* 1 : 1190–92.
6. Pedrinelli R, Giampietro O, Carmassi F, Matteucci E, Talarico L, Morale M, et al. 'Microalbuminuria and endothelial dysfunction in essential hypertension', 1994; *Lancet* 344:14–18.
7. Cardiovascular diseases; WHO health topic page on cardiovascular diseases.
8. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications. Part 1: Diagnosis and Classification of Diabetes Mellitus. WHO, Geneva, 1999.

9. Khan AKA, Mahatab H, Grant J,Stewart M,Ahemad D, Definition, Presentation,Diagnosis and Classification of Diabetes Mellitus, Diabetic Association of Bangladesh. 2011; 30.

10. Standard of medical care in diabetes,'American Diabetes Association,' *DiabetesCare*. 2013: 36(1): S11-S66.

11. Farshchi A, Esteghamati A, Sari AA, Kebriaeezadeh A, Abdollahi M, Dorkoosh FA,et al. 'The cost of diabetes chronic complications among Iranian people with type 2 diabetes mellitus', *Journal of Diabetes & Metabolic Disorders*. 2014: 13: 42.

12. Masum N, Nasrin F, Neaz S, Tamanna N, Islam KS, Chowdhury MR, et al. **'**Association of Uric acid with type II diabetes'*,IRJALS,* 2012: 1(4):13.

14. Venugopal S,Iyer UM, 'Risk Factor Analysis and Prevalence of Microalbuminuria among Type 2 Diabetes Mellitus Subjects: The Need for Screening and Monitoring Microalbumin', *Asian j. Exp. Biol. Sci*. 2010: 1(3): 652-59.

15. Alharf, Adel Abdullah, Prevalence of and clinical characteristics associated with microalbuminuria in hypertension. PhD thesis. 2012.

16. Ibrahim IH, Zaidan HK,Ameri QMA, Ewadh MJ,Saadi AH,'The Prevalence of Microalbuminuria in Type 2 Diabetes Mellitus Patients in Al-Husain Hospital in Karbala Province-Iraq', *Research in Biotechnology*. 2012: 3(2): 14-21.

17. Wu AY, Kong NC, De Leon FA, Pan CY, Tai TY, Yeung VT et al. 'An alarmingly high prevalence of diabetic nephropathy in Asian type 2 diabetic patients: theMicroAlbuminuria Prevalence (MAP) Study', *Diabetologia*. 2005: 48(1): 17-26.

18. Prasanna B.'Association and predication between prolonged QT interval and microalbuminuria in patients of type II diabetes mellitus- a cross sectional study', *J.J.M Medical college devengere.*2011: 1-117.