

## ORIGINAL ARTICLE

# Association of Cardiovascular Disease with Micro Albuminuria in Type 2 Diabetes Mellitus

WALI GUL<sup>1</sup>, WAHEED IQBAL<sup>2</sup>, MIRZA REHAN BAIG<sup>3</sup>, MOHSIN EJAZ<sup>4</sup>, AAMENA GARDAZI<sup>5</sup>, KASHIF ALI SAMIN<sup>6</sup>

<sup>1</sup>District Medical Specialist, DHQ Category A Hospital, Batkhela.

<sup>2</sup>FCPS (Medicine) Associate Professor Department of Medicine Divisional Headquarters Teaching hospital Mirpur/ Mohtarma Benazir Bhutto Shaheed Medical College Mirpur

<sup>3</sup>MRCP (UK) Assistant Professor Department of Medicine, Hamdard University hospital Karachi.

<sup>4</sup>PGR, department of Gastroenterology CMH, Multan

<sup>5</sup>Registrar Internal Medicine MMDC and Ibn-e-Siena hospital Multan

<sup>6</sup>Assistant Professor Family Medicine Khyber Medical University Peshawar

Correspondence to: Dr Wali Gul, Email: [waligul.kth@gmail.com](mailto:waligul.kth@gmail.com), Cell No: +92 332 9497556

## ABSTRACT

**Objective:** The aim of this study is to determine the prevalence of cardiovascular disease with micro albuminuria in type 2 diabetes mellitus.

**Study Design:** Observational study

**Place and Duration:** Study was carried out in medicine department of DHQ category A hospital Batkhela and Combined Military Hospital, Multan for duration of six months from January 2020 to June 2020.

**Methods:** Total 120 patients of both genders diagnosed diabetes 2 mellitus were presented in this study. Patients were aged between 20-80 years. Patients' details demographics were recorded after taking written consent. Prevalence of cardiovascular disease with microalbuminuria was assessed by statistical analysis. Microalbuminuria was diagnosed among patients if urinary albumin excretion was >30mg/g and in normal albuminuria urinary albumin excretion was <30mg/g. Complete data was analyzed by SPSS 20.0 version.

**Results:** Out of 120, 66 (55%) were males and 54 (45%) were females. Mean age of the patients were 45.71±16.9 years with mean BMI 26.14±9.22 kg/m<sup>2</sup>. Cardiovascular disease found in 90 (75%) cases. We found that 80 (66.7%) patients had microalbuminuria with mean ACR 160.4±74.6 mg/gm while rest of the patients 40 (33.3%) had normal albuminuria 19.14±5.4 mg/gm. Among 90 cases of cardiovascular disease frequency of microalbuminuria was 65 (72.22%) and among 30 diabetes patients of non- cardiovascular disease frequency of microalbuminuria were 15 (50%). Microalbuminuria was found significantly higher in patients of cardio vascular disease and increased systolic and diastolic blood pressure compared to normoalbuminuric patients. In patients with microalbuminuria, blood glucose and glycosylated hemoglobin have increased dramatically.

**Conclusion:** We concluded in this study that the prevalence of cardiovascular disease with micro albuminuria in type 2 diabetes mellitus was significantly high <0.05 with increased systolic diastolic pressure and fasting blood glucose as compared to normal albuminuria.

**Keywords:** Microalbuminuria, Normal albuminuria, Type 2 Diabetes, Cardio vascular disease

## INTRODUCTION

The early clinical discovery of diabetic nephropathy is increased urine protein excretion[1-3]. The urine dipstick is a reasonably insensitive proteinuria marker that becomes positive until a protein excretion is greater than 300-500 mg/day. It is a more sensitive procedure to use a particular test for albumin. A consistent 30-300 mg/d value is called micro albuminuria and is frequently indicated by suggestive diabetic nephropathy in diabetic patients. The normal rate of excretion is less than 20 mg/day (unless there is some coexistent renal disease). 1 Over-threshold proteinuria value exceeding 300 mg is considered. 5 Early stage of diabetic nephropathy is regarded as Microalbuminuria. [3-6]

Risk factors are defined as variants which are (reportedly) causally linked to cardiovascular disease whereas risk factors, such as a pathophysiological mechanism caused by atherothrombosis and because they are strongly linked with an unknown (and unmeasured) risk factor, are indirectly related to a cardiovascular disease. Microalbuminuria is a widely accepted, powerful and independent cardiovascular disease risk factor for diabetic people. In a systemic assessment, for instance, Dinneen and Gerstein[7] have shown an increased risk of

cardiovascular death compared to normalalbuminuria to increase microalbuminuria among persons with Type 2 diabetes at 2.4-fold (95% confidence interval [CI] 1.8 to 3.1). Moreover, hypertensive people (no diabetes) and the community as a whole have similar associations [8-9]. Maintaining the link between microalbuminuria and cardiovascular risk, the recent investigations have added three new findings. First, there are no traditional thresholds for microalbuminuria association (that is, 2.5mg/mmol in men, 3.5 mg/mmol in women, or equal urinary albumin excretion rates) but rather, there is a much lower threshold of 1mg/mmol creatinine, or even lower thresholds. Instead of this, there is a strong linkage between the urinary albumin excretion and the cardiovascular disease risk. [10,11] Second, advancement of microalbuminuria in persons with diabetes has been found to be associated with a further increase in the risk of cardiovascular disease, regardless of the initial release of urine albums[12]. 3. Any decay in urinary albumin excretion during therapy was associated with a reduction in the risk of the Primary Composite Endpoint (cardiovascular mortality, stroke, and myocardial) during the Losartan Intervention study during the 4.8 year treatment in 8206 patients suffering from hypertension and left ventricular hypertrophy (LIFE).[13,14]

These relationships are wider than microalbuminurias, between urine excretion and cardiovascular disease. For instance, Samuelsson et al.[15] revealed in a 10-year follow-up research that macroalbuminuria (i.e. albumin excretory over the microalbuminuria threshold) was related with nearly three times hypertensive men with elevated cardiovascular risk. Any decrease in albuminuria was significantly linked to the lower risk of heart and renal effects in the reduction of endpoints in NIDDM in the angiotensinII study by Antagonist Losartan (RENAAL). [16]

## MATERIAL AND METHODS

This observational study was conducted at medicine department of DHQ category A hospital Batkhela and Combined Military Hospital, Multan for duration of six months from January 2020 to June 2020. The study was comprised of 120 type 2 diabetes mellitus patients. Patients' details demographics were recorded after taking written consent. Patients who had other medical illness and those did not give any written consent were excluded from this study.

Patients were aged between 20-80 years. Prevalence of cardiovascular disease with microalbuminuria was assessed by statistical analysis. Microalbuminuria was diagnosed among patients if urinary albumin excretion was >30mg/g and in normal albuminuria urinary albumin excretion was <30mg/g. Categorical variables were assessed by frequency and percentage but descriptive variables were calculated by standard deviation. Complete data was analyzed by SPSS 20.0 version.

## RESULTS

Out of 120, 66 (55%) were males and 54 (45%) were females. Mean age of the patients were  $45.71 \pm 16.9$  years with mean BMI  $26.14 \pm 9.22$  kg/m<sup>2</sup>. Mean duration of diabetes was  $6.08 \pm 9.64$  years. Most of the patients 78 (65%) were from the age group > 40 years and the rest were 42 (35%) <40 years of age. (table 1)

Table 1: Baseline details of enrolled cases

Characteristics	Frequency	%age
Gender		
Male	66	55
Female	54	45
Mean age (years)	$45.71 \pm 16.9$	
Mean BMI	$26.14 \pm 9.22$	
Mean Duration of the Diabetes (years)	$6.08 \pm 9.64$	
Age group		
<40 years	78	65
>40 years	42	35

Table 2: Prevalence of cardiovascular disease and microalbuminuria among patients

Characteristics	Frequency (120)	%age
Cardiovascular disease		
Yes	90	75
No	30	25
Microalbuminuria (>30mg/g)		
Yes	80	66.7
No	40	33.3
Mean ACR		
Microalbuminuria	$160.4 \pm 74.6$	
Normal albuminuria	$19.14 \pm 5.4$	

Cardiovascular disease found in 90 (75%) cases. We found that 80 (66.7%) patients had microalbuminuria with mean ACR  $160.4 \pm 74.6$  mg/gm while rest of the patients 40 (33.3%) had normal albuminuria  $19.14 \pm 5.4$  mg/gm. (table 2)

Among 90 patients of cardiovascular disease HTN was the most common found in 27 (30%) cases followed by HTN+Stroke 22 (24.44%). (Table 3)

Table 3: Association of cardio vascular diseases among patients

Characteristics	Frequency (n=90)	%age
HTN	27	30
HTN+Stroke	22	24.4
HTN+IHD	21	23.3
HTN+IHD+Stroke	14	15.5
IHD	2	2.2
Stroke	2	2.2
IHD+Stroke	2	2.2

Among 90 cases of cardiovascular disease frequency of microalbuminuria was 65 (72.22%) and among 30 diabetes patients of non- cardiovascular disease frequency of microalbuminuria were 15 (50%). Microalbuminuria was found significantly higher in patients of cardiovascular disease and increased systolic and diastolic blood pressure compared to normoalbuminuric patients. In patients with microalbuminuria, blood glucose and glycosylated hemoglobin have increased dramatically. (Table 4)

Table 4: Prevalence of microalbuminuria among type 2 diabetes patients with cardiovascular disease

Cardiovascular disease	Cardiovascular disease	Non Cardiovascular disease
Microalbuminuria >30mg/g	65 (72.22%)	15 (50%)
Normal albuminuria <30mg/g	25 (27.8%)	15 (50%)
Total	90	30
Systolic BP	135	140
Diastolic BP	90	92

## DISCUSSION

Different epidemiological studies have revealed significant variance in microalbuminuria prevalence. [17] In this observational study, 120 patients of type 2 diabetes mellitus were enrolled. Majority of the patients were males 55% as compared to females 45%. Mean age of the patients were  $45.71 \pm 16.9$  years with mean BMI  $26.14 \pm 9.22$  kg/m<sup>2</sup>. These findings were comparable to the previous some studies. [18] Most of the patients 78 (65%) were from the age group > 40 years and the rest were 42 (35%) <40 years of age and mean duration of diabetes was  $6.08 \pm 9.64$  years. [19]

Microalbuminuria was diagnosed among patients if urinary albumin excretion was >30mg/g and in normal albuminuria urinary albumin excretion was <30mg/g. We found that 80 (66.7%) patients had microalbuminuria with mean ACR  $160.4 \pm 74.6$  mg/gm while rest of the patients 40 (33.3%) had normal albuminuria  $19.14 \pm 5.4$  mg/gm. Cardiovascular disease found in 90 (75%) cases. Among 90 patients of cardiovascular disease HTN was the most common found in 27 (30%) cases followed by HTN+Stroke 22 (24.44%). Comparable to the previous some studies in

which microalbuminuria were highly associated with cardiovascular disease. [18-20]

Among 90 cases of cardiovascular disease frequency of microalbuminuria was 65 (72.22%) and among 30 diabetes patients of non- cardiovascular disease frequency of microalbuminuria were 15 (50%). Microalbuminuria was found significantly higher in patients of cardiovascular disease and increased systolic and diastolic blood pressure compared to normoalbuminuric patients. In patients with microalbuminuria, blood glucose and glycosylated hemoglobin have increased dramatically. Similarly, Prasanna (2011) showed an increased incidence of microalbuminuria as the duration of diabetes increases. [21] A MAP research revealed that microalbuminuria was high in diabetic Asian type 2 hypertensive subjects with high prevalence (39.8%) MAP research MAP (Wu et al. 2005). [22] The microalbuminuria prevalence was less than our studies in several research. Gupta et al. have reported 26.6% prevalence in 65 north indian non-proteinuric patients,[23] whereas John et al. reported 19.7% prevalence in a tertiary hospital in the cities of Vellore, South India,[24] and Vijay et al. have reported that 15.7% of 600 type 2 diabetic patients studied in a diabetic center in the village of Chennai have proteinuria. [25] 26% of Pima Indians.

Microalbuminuria was high among men in the present study. Earlier researches have shown that microalbuminuria is more prevalent in men than to women. Since women have a lower excretion than men, however, there is an issue in comparing the prevalence among the genders with the use of the albumin creatinine ratio. Some authors therefore have a lower men threshold than women. Blood hypertension and poor glycaemic management are the causal risk factors for microalbuminuria. Duration of diabetes, men and previous retinopathy as key risk factors for microalbuminuria have been shown in several research. [26]

Microalbuminuria has been proven to be an important predictor for cardiovascular disease progression in type 2 DM. Duration of DM increases the occurrence of cardiovascular disorders in patients type 2 DM. HbA1c in most people is also elevated. In most unmanaged DM the presence of microalbuminuria steadily increases with the duration of DM and especially over 5 years. In patients with type 2 DM, microalbuminuria is found to be heavily linked to cardiovascular conditions, and cardiovascular disorders are 3 times more likely.

## DISCUSSION

We concluded in this study that the prevalence of cardiovascular disease with micro albuminuria in type 2 diabetes mellitus was significantly high  $<0.05$  with increased systolic diastolic pressure and fasting blood glucose as compared to normal albuminuria.

## REFERENCE

1. Mogensen CE. Prediction of clinical diabetic nephropathy in IDDM patients. Alternative to microalbuminuria? *Diabetes* 1990;39:761.
2. Ruggeneti P, Remuzzi G. Nephropathy of type 2 diabetes mellitus. *J Am Soc Nephrol* 1998;9:2157

3. Ismail N, Becker B, Strzelczyk P, Ritz E. Renal disease and hypertension in non insulin dependent diabetes mellitus. *Kidney Int* 1999;55:1
4. Mogensen CE, Steffes MW, Deckert T. Functional and morphological renal manifestation in diabetes mellitus. *Diabetologia* 1981;21:89-93
5. Viberti GC, Keen H. The pattern of proteinuria in diabetes mellitus: Relevance of pathogenesis and prevention of diabetes nephropathy. *Diabetes* 1984;33:686-92.
6. Parving HH, Gall MA, Skott P. Prevalence and causes of albuminuria non insulin dependent diabetic patients. *Kidney Int* 1990;41:758-86.
7. Dinneen SF, Gerstein HC: The association of microalbuminuria and mortality in non-insulin-dependent diabetes mellitus. A systematic overview of the literature. *Arch Intern Med* 157: 1413-1418, 1997
8. Jensen JS, Feldt-Rasmussen B, Strandgaard S, Schroll M, Borch-Johnsen K: Arterial hypertension, microalbuminuria, and risk of ischemic heart disease. *Hypertension* 35: 898 – 903, 2000
9. Gerstein HC, Mann JFE, Yi Q, Zinman B, Dinneen SF, Hoogwerf B, Halle JP, Young J, Rashkwo A, Joyce C, Nawaz S, Yusuf S; for the HOPE Study Investigators: Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. *JAMA* 286: 421– 426, 2001
10. Volpe M, Cosentino F, Ruilope LM: Is it time to measure microalbuminuria in hypertension? *J Hypertens* 21: 1213– 1220, 2003
11. Klausen K, Borch-Johnsen K, Feldt-Rasmussen B, Jensen G, Clausen P, Scharling H, Appleyard M, Jensen JS: Very low levels of microalbuminuria are associated with increased risk of coronary heart disease and death independently of renal function, hypertension, and diabetes. *Circulation* 110: 32–35, 2004
12. Arnlov J, Evans JC, Meigs JB, Wang TJ, Fox CS, Levy D, Benjamin EJ, D'Agostino RB, Vasan RS: Low-grade albuminuria and incidence of cardiovascular disease events in non-hypertensive and non-diabetic individuals. *Circulation* 112: 969 –975, 2005
13. Ibsen H, Olsen MH, Wachtell K, Borch-Johnsen K, Lindholm LH, Mogensen CE, Dahlöf B, Devereux RB, Beevers G, de Faire U, Fyhrquist F, Julius S, Kjeldsen SE, Lederballe-Pedersen O, Nieminen MS, Omvik P, Oparil S, Wan Y: Reduction in albuminuria translates to reduction in cardiovascular events in hypertensive patients: Losartan Intervention for Endpoint Reduction in Hypertension Study. *Hypertension* 45: 198 – 202, 2005
14. Ibsen H, Wachtell K, Olsen MH, Borch-Johnsen K, Lindholm LH, Mogensen CE, Dahlöf B, Devereux RB, Beevers G, de Faire U, Fyhrquist F, Julius S, Kjeldsen SE, Lederballe-Pedersen O, Nieminen MS, Omvik P, Oparil S, Wan Y: Does albuminuria predict cardiovascular outcome on treatment with losartan versus atenolol in hypertension with left ventricular hypertrophy? *J Hypertens* 22: 1805– 1811, 2004
15. Samuelsson O, Wilhelmsen L, Elmfeldt D: Predictors of cardiovascular morbidity in treated hypertension: Results from the Primary Preventive Trial in Gotenborg, Sweden. *J Hypertens* 3: 167–176, 1985
16. de Zeeuw D, Remuzzi G, Parving HH, Keane WF, Zhang Z, Shahinfar S, Snapinn S, Cooper ME, Mitch WE, Brenner BM: Proteinuria, a target for renoprotection in patients with type 2 diabetic nephropathy: Lessons from RENAAL. *Kidney Int* 65: 2309 –2320, 2004
17. Guo, L., Cheng, Y., Wang, X. *et al.* Association between microalbuminuria and cardiovascular disease in type 2 diabetes mellitus of the Beijing Han nationality. *Acta Diabetol* 49, 65–71 (2012)
18. Abdulrahman Al-Shaikh et al prevalence of microalbuminuria in type 2 diabetes mellitus at a diabetic clinic in king

- abdulaziz university hospital. Pak J Med Sci April 2007 Vol. 23 No. 2 223-226
19. MdJahirul Haque<sup>1</sup> , Md. Nazrul Islam<sup>2</sup> , Md. Zakaria Al Aziz<sup>3</sup> , Shah Mohammad Ashrafuzzaman<sup>4</sup> , Gobindo Chandra Banik<sup>5</sup> , AKM Sajedur Rahman<sup>6</sup> , Sarmistha Biswas<sup>7</sup> , HAM NazmulAhasan. Association of Cardiovascular Disease with Micro Albuminuria in Type 2 Diabetes Mellitus - Study in A Tertiary Care Hospital. 20 September 2020. JOM Vol. 21, No. 2
  20. Jie W, Zhiqiang L (2005) A epidemiological cross-sectional survey of microalbuminuria and risk factors in type 2 diabetic patients. Clin Med J Chin 12(5):859–861
  21. PrasannaB. '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.
  22. 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.
  23. Gupta DK, Verma LK, Khosla PK, et al. The prevalence of microalbuminuria in diabetes: a study from north India. Diabetes Res ClinPract 1991;12:125–8.
  24. John L, Rao PS, Kanagasabapathy AS. Prevalence of diabetic nephropathy in non insulin dependent diabetes. Indian J Med Res 1991;94:24–9
  25. Vijay V, Snehalatha C, Ramachandran A, et al. Prevalence of proteinuria in non-insulin dependent diabetes. J Assoc Physicians India 1994;42:792–4
  26. Nelson RG, Kunzelman CL, Pettit DJ,et al. Albuminuria in type 2 (non-insulin-dependent) diabetes mellitus and impaired glucose