

RELATIONSHIP OF GLYCEMIC CONTROL WITH PREVALENCE OF MICROALBUMINURIA IN DIABETIC PATIENTS

Purdil Khan, Momin Khan, Aziz Ahmad, Abdul Ahad, Wasil Khan

Department of Medicine, Saidu Group of Teaching Hospitals, Swat, Pakistan

ABSTRACT

Background: Microalbuminuria is a renal marker of generalized vascular endothelial damage and early atherosclerosis. Patients with microalbuminuria are at increased risk of microvascular and macrovascular complications of diabetes mellitus like myocardial infarction, stroke and nephropathy. Poor glycemic control increases the risk of microalbuminuria. This study was conducted to determine the frequency of microalbuminuria in type 2 diabetes and compare the frequency of microalbuminuria in poor and good glycemic control in type 2 diabetes.

Material & Methods: One Hundred and twenty-two type 2 diabetic patients were included in the study. Data on age, gender, duration of diabetes, microalbuminuria and HbA1c were recorded. Urine and blood samples were collected and analyzed for microalbuminuria, blood glucose and HbA1c. All patients of both genders with type 2 diabetes for over 2 years were selected in this study. Patients with other causes of proteinuria were excluded.

Results: Out of 122 cases 58(47.5%) were male and 64(52.5%) were female. Average age of patients was 46.87 years and average duration of diabetes was 7.16 years. Over all prevalence of microalbuminuria was 29.5%. Patients with poor glycemic control and good glycemic control have frequency of microalbuminuria of 35.9% and 10% respectively.

Conclusion: Uncontrolled diabetes is strongly associated with prevalence of microalbuminuria. Screening for microalbuminuria and HbA1c test should be done both in newly and already diagnosed type 2 diabetic patients as an early marker of renal dysfunction and glycemic control.

Key Words: Microalbuminuria, HbA1c, Diabetes mellitus.

This article may be cited as: Khan P, Khan M, Ahmad A, Adad A, Khan W. Relationship of glycemic control with prevalence of microalbuminuria in diabetic patients. *Gomal J Med Sci* 2012; 10: 201-4.

INTRODUCTION

Microalbuminuria (MA) is an earliest marker of nephropathy and cardiovascular disease (CVD) in patients with diabetes,¹ which is an albumin excretion rate of 20-200 $\mu\text{g}/\text{min}$ on a timed collection. Although microalbuminuria is predictive of worsening microvascular disease in the kidney (5-10% per year progress to overt diabetic nephropathy), an increased albumin excretion rate (AER) reflects a generalized abnormality of vascular function and is associated with 2-4 fold increases in cardiovascular and all-cause mortality.² Microalbuminuria requires ultrastructural changes rather than alterations in glomerular pressure or filtration rate alone.³

There is some evidence that irrespective of the duration and type of diabetes the damage to the kidney can be avoided if good glycemic control is achieved.⁴ proportion of microalbuminuria is high (72%) in Pakistan reflecting poor glycemic control in our set up.⁵

Measurement of HbA1c is used to determine average glycemic control over an 8-12 week period, and HbA1c level has been linked to development of microvascular complications.⁶ The Diabetes Control and Complications Trial (DCCT) and United Kingdom Prospective Diabetic Study (UKPDS) have demonstrated that intensive glycemic control significantly reduces the risk for development of microalbuminuria in type 2 diabetics. According to DCCT strict glycemic control (HbA1c < 7) had a relative risk reduction for development of microalbuminuria by 34%. In the UKPDS, a difference in HbA1c of 0.9% reduces the risk for development of microalbuminuria by 30%. Therefore, a target HbA1c <7 should be recommended in all patients with type 2 diabetes.⁷

Corresponding Author:

Dr. Purdil Khan
Swat Medical Complex,
Saidu Sharif, Swat
e-mail: dr.purdil@gmail.com

This study was designed to determine the frequency of microalbuminuria in patients with type 2 diabetes in this part of the country and compare this among those with good and poor glycemic control.

MATERIAL AND METHODS

This cross sectional study was conducted in the Medical Unit of Saidu Group of Teaching Hospitals, Saidu Sharif, Swat from June 2011 to May 2012. One hundred and twenty two known type 2 diabetic patients were enrolled in the study by non probability convenient sampling.

Demographic data and history regarding name, age, sex, duration of DM was taken. According to WHO criteria diabetes type 2 was diagnosed if fasting blood sugar was more than 126 mg/dl or random blood sugar was more than 200 mg/dl and not insulin dependent. Venous blood was collected after 12 hours fasting for HbA1c. Twenty-four hours urine was collected for estimation of microalbuminuria.

In order to measure urinary albumin concentration accurately, patients were given necessary instructions regarding the collection of urine samples. When no evidence of infection and/or haematuria was found in the urinalysis, urine samples were examined for microalbuminuria. Urinary albumin was measured with an autoanalyzer (analyzer medical system, Italy) using Randox kits (urinary albumin measured with immunoturbidimetry method, UK). A second 24-hours urine sample was obtained and examined for microalbuminuria, if the first measurement exceeded 30mg of albumin. The diagnosis of microalbuminuria was confirmed when >30 mg/dl albumin was found in the second sample. Twenty-four hours urinary albumin concentration of <30 mg were considered as normal (normoalbuminuria), 30–300 mg as microalbuminuria. HbA1c was carried out and labeled good glycemic control when found less than 7 and greater than or equal to 7 were considered poor glycemic control. Patients with hypertension and urinary tract infection were excluded because these are the confounders. All the investigations were done by single pathologist to control the confounder and to make the study results unbiased.

SPSS version 16 was used for the analysis of data. Mean and standard deviation was calculated for age, and duration of diabetes. Frequency and percentage was calculated for gender. HbA1c and microalbuminuria stratifications were done with regards to age, gender and duration of diabetes to see the effect of these on outcomes. Chi-square test was applied between microalbuminuria and HbA1c and cross tabulation tool was used to see the relation between HbA1c and microalbuminuria. P Value < 0.05 was considered as significant.

RESULTS

A total of 122 patients were enrolled in this study; 58 (47.54%) were male and 64 (52.46%) female with a ratio of 1:1.03. Sex distribution of microalbuminuria showed that 22.4% male while 35.9% female patients had microalbuminuria. This gender wise difference was not statistically significant with p-value=0.102. (Table 1)

Average age of the patients was 46.87+3.2 years with the range of 30-50 years. Age wise distribution of microalbuminuria is given in Table 2. It shows percentages of different age groups having microalbuminuria. Chi square test showed that microalbuminuria had insignificant role over the age of patients with p=0.797 but it did show that with increase in age, the incidence of microalbuminuria also increased. Average duration of diabetes was 7.16+3.18 years. Chi square test showed that microalbuminuria had significant role over duration of diabetes mellitus.

Results of HbA1c wise distribution of microalbuminuria has been shown in the graphic

Table 1: Sex-wise distribution of microalbuminuria. (n=122)

Sex	Microalbuminuria		Total	P-value
	Yes	No		
Male	13 22.4%	45 77.6%	58 100.0%	0.10
Female	23 35.9%	41 64.1%	64 100.0%	
Total	36 29.5%	86 70.5%	122 100.0%	

Table 2: Age wise distribution of microalbuminuria.

Age	Microalbuminuria		Total	P-value
	Yes	No		
30-35	7 5.7%	11 9.1%	18 14.8%	0.79
36-40	9 7.4%	26 21.3%	35 28.7%	
41-45	10 8.2%	25 20.5%	35 28.7%	
46-50	10 8.2%	24 19.7%	34 27.9%	
Total	36 29.5%	86 70.5%	122 100.0%	

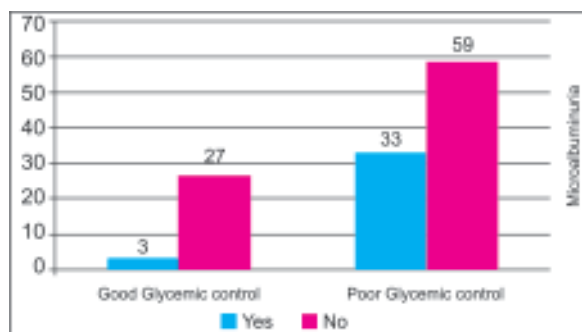


Fig 1: Microalbuminuria and HbA1c.

form showing over all proportion of microalbuminuria as 29.5%. Chi square test shows that microalbuminuria is significantly high in poor glycaemic control patients with p -value=0.007. (Fig. 1).

DISCUSSION

Diabetes mellitus is a global health problem. Majority of patients are in the young and middle age group.⁸ The prevalence of diabetes mellitus is high in Pakistan ranging from 3-14% which varies in the Urban and Rural areas and is a major health problem in Pakistan.⁹

Microalbuminuria which is an early marker of diabetic nephropathy may be present at diagnosis of type 2 diabetes. It progresses to overt nephropathy and eventually leads to decline in glomerular filtration rate and ultimately to end stage renal disease or premature cardiovascular mortality.¹⁰

The frequency of Microalbuminuria in the present study was 29.5%. Similar results have also been shown by other studies with slight variation in the frequency of microalbuminuria ranging from 24-34%.¹¹⁻¹⁵ This slight variation in the frequency may be due to different factors like variation in definition of diabetes, stage of the disease, method of assessment and ethnic susceptibility to develop nephropathy.

Another finding in this study was that females were major sufferers with 23 cases while males were 13. Female dominance has also been noted by other studies.^{16,17}

High frequency of diabetes was found in patients between 40–50 years of age. Similar results were also reported by another study.¹⁴

Increase level of microalbuminuria is associated with increase rate of progression of kidney damage, ultimately leading to end stage renal disease. Microalbuminuria also increases cardiovascular morbidity and mortality², therefore screening of type 2 diabetics for microalbuminuria should begin at the time of diagnosis to retard the progression and perhaps reversion to normoalbuminuria at an early stages of disease. Once sustained microal-

buminuria develops then urinary albumin excretion rate increases by 10-20% per year to overt nephropathy over a period of 10-15 years. The rate of fall of glomerular filtration rate in patients of diabetes with overt nephropathy in type 2 diabetes is variable ranging from 2–20ml/min/yr.¹⁰ Therapeutic and non-therapeutic intervention can reverse the process at this stage but if untreated then will lead to end stage renal disease and cardiovascular mortality.

During the first 5 years of diabetes, microalbuminuria rarely found suggesting that it is a marker of early glomerular damage. Duration of diabetes is an important factor which strongly correlates with increase frequency of microalbuminuria. In the present study 31 diabetic patients had microalbuminuria even when the duration of diabetes was less than 11 years. These are the patients who can benefit from the screening Programme for microalbuminuria to prevent or delay nephropathy as well as other complications. The results of this study have shown positive correlation between the duration of diabetes and frequency of microalbuminuria. A significant correlation between microalbuminuria and duration of diabetes had also been shown by other studies.^{18,19} Early detection of diabetic nephropathy is important so that strategies could be made to prevent progression to end stage renal disease.

HbA1c, which is a measure of erythrocyte haemoglobin glycation and reflects mean glycaemic value for the previous 3 recent months;²⁰ have also been measured in this study. The results of this study have shown positive correlation between microalbuminuria and glycaemic control as shown by the high frequency of microalbuminuria (33%) in poor glycaemic control (HbA1c >7) group as compared to only 10% of microalbuminuria in good glycaemic control (HbA1c <7) group. A significant correlation between microalbuminuria and glycaemic control have also been shown by other studies.^{13,16,18,19}

Good glycaemic control (HbA1c <7) reduces both the incidence and progression of microalbuminuria.^{19,21,22} Early diagnosis and treatment of Diabetic patients aiming for a good glycaemic control will prevent the development of nephropathy and could also produce financial saving as well as better patient outcomes.^{23,24}

CONCLUSION

Uncontrolled diabetes is strongly associated with prevalence of microalbuminuria. Screening for microalbuminuria and HbA1c test should be done both in newly and already diagnosed type 2 diabetic patients as an early marker of renal dysfunction and glycaemic control.

REFERENCES

1. Pan CY, Soegondo S, Prodjosudjadi W, Suwan-walaikorn S, Lim SC, Chan KW, et al. Prevalence of albuminuria and cardiovascular risk profile in a referred cohort of patients with type 2 diabetes: an Asian perspective. *Diabetes Technol Ther* 2008; 10: 397-403.
2. Donnelly R, Yeung JM, Manning G. Microalbuminuria: a common independent cardiovascular risk factor, especially but not exclusively in type 2 diabetes. *J Hypertens Suppl* 2003; 21: 7-12.
3. Satchell SC, Tooke JE. What is the mechanism of microalbuminuria in diabetes: a role for the glomerular endothelium? *Diabetologia* 2008; 51: 714-25.
4. Ghafoor F, Bano KA, Malik T, Mahmood S, Khan A. Microalbuminuria as an indicator of kidney function among Diabetics. *J Coll physicians Surg Pak* 2004; 14: 670-2.
5. Shaukat A, Arain TM, Shahid A. Microalbuminuria: Incidence in patients of diabetes mellitus at Bahawalpur. *Pak J Pathol* 2005; 16: 17-21.
6. Jesudason DR, Dunstan K, Leong D, Wittert GA. Macrovascular Risk and Diagnostic Criteria for Type 2 Diabetes. *Diabetes Care* 2003; 26: 485-90.
7. Fioretto P, Bruseghin M, Berto I, Gallina P, Manzato E, Mussap M. Renal protection in diabetes, role of glycemic control. *J Am Soc Nephrol* 2006; 17: 86-9.
8. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projection for 2030. *Diabetes care* 2004; 27: 1047-53.
9. Shera AS, Jawad F, Maqsood A. Prevalence of diabetes in Pakistan: *Diab Res Clin Pract* 2007; 76: 219-22.
10. American Diabetes Association. Diabetic nephropathy. *Diabetes Care* 2003; 26 (Suppl 1): S94-8.
11. Yokoyama H, Kawai K, Kobayashu M. Microalbuminuria is common in Japanese type 2 diabetic patients: a nationwide survey from Japan. Diabetes clinical data management study group (JDDM 10). *Diabetes Care* 2007; 30: 989-92.
12. Venugopal S, Iyer UM. Risk factors analysis and prevalence of microalbuminuria among type 2 diabetes mellitus subjects: the need for screening and monitoring microalbuminuria. *Asian J Exp Bio sci* 2010; 1: 652-9.
13. Gerstein HC, Mann JFE, Pogue J, Dinneen SF, Halle JP, Hoogwerf B, et al. Prevalence and determinants of microalbuminuria in high risk diabetic and non-diabetic patients in the Heart Outcomes Prevention Evaluation Study. *Diabetes Care* 2000; 23 (Suppl 2): S35-9.
14. Naz S, Sadruddin A, Khanum A, Osmani R. Frequency of microalbuminuria in diabetic patients of Islamabad and Rawalpindi. *Pak J Med Res* 2007; 46124-7.
15. Ahmadani MY, Fawwad A, Basit A, Hydri ZI. Microalbuminuria prevalence study in hypertensive patients with type diabetes in Pakistan. *J Ayub Med Coll* 2008; 20: 117-20.
16. Sigdel M, Rajbhandari N, Basnet S, Nagila A, Basnet P, Tamrakar BK. Microalbuminuria among type 2 diabetes mellitus patients in Pokhara, Nepal. *Nepal Med Coll J* 2008; 10: 242-5.
17. Pruijm MT, Madeline G, Riesen WF, Burnier M, Bovet P. Prevalence of microalbuminuria in the general population of Seychelles and strong association with diabetes and hypertension independent of renal markers. *J Hypertens* 2008; 26: 871-7.
18. Young BA, Katon WJ, Korff MV, Simon GE, Lin EHB, Ciechanowski PS, et al. Racial and ethnic differences in microalbuminuria prevalence in a diabetes population: The Pathways Study. *J Am Soc Nephrol* 2005; 16: 219-28.
19. Sheikh SA, Baig JA, Iqbal T, Kazmi T, Baig M, Husain SS. Prevalence of microalbuminuria with relation to glycemic control in type-2 diabetic patients in Karachi. *J Ayub Med Coll Abbotabad* 2009; 21: 83-6.
20. Saudek CD, Kalyani RR, Derr RL. Assessment of glycaemia in Diabetes mellitus: Hemoglobin A1c. *J Assoc Physician India* 2005; 53: 299-304.
21. Jerums G, Macisaac RJ. Treatment of microalbuminuria in patients with type 2 diabetes mellitus. *Treat Endocrinol* 2002; 1: 163-73.
22. Vora JP, Ibrahim HA, Bakris GL. Responding to the challenge of diabetic nephropathy: the historic evolution of detection. Prevention and management. *J Hum Hypertens* 2000; 14: 667-85.
23. CDC. Number of Americans with diabetes rises to nearly 26 million. Available at: http://www.cdc.gov/media/releases/2011/p0126_diabetes.html.
24. Narayan KM, Boyle JP, Thompson TJ, Sorensen SW, Williamson DF. Life time risk for diabetes mellitus in the United States. *JAMA* 2003; 290: 1884-90.

CONFLICT OF INTEREST
 Authors declare no conflict of interest.
GRANT SUPPORT AND FINANCIAL DISCLOSURE
 None declared.