

ORIGINAL ARTICLE

FREQUENCY OF ALBUMINURIA IN DIABETIC PATIENTS PRESENTING WITH MACROVASCULAR COMPLICATIONS

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Background: Diabetes mellitus is major cause of morbidity and premature mortality from its long term complications such as cardiovascular disease, blindness, renal failure, amputation and stroke. The study was conducted to determine the frequency of albuminuria in diabetic patients presenting with macro-vascular complications like myocardial infarction (MI) and stroke. **Methods:** This descriptive study was conducted at Ayub Medical College, Abbottabad from December 2010 to May 2011. Total 88 diabetic patients admitted with macro-vascular disease were included in this study. The patients were subjected to two urine specimen's examination, one for routine examination for infection and dipstick analysis for albuminuria. Second was tested for albumin was tested in the urine. **Results:** Out of 88 patients with a mean 47.12 ± 7.58 years, 39 (44.32%) were female while 49 (55.68%) were male. Overall albuminuria was detected in the urine of 81 out of total 88 patients (92%) when tested by heating method whereas it was detected in 41 (46.6%) cases by the dipstick method. **Conclusion:** Frequency of albuminuria is much higher in diabetic population with macro-vascular complications; hence albumin in the urine of diabetic patient can be regarded as an indicator for impending macro-vascular complications of diabetes.

Keywords: Diabetes mellitus, macro-vascular disease, albuminuria, complications, CVA

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INTRODUCTION

Diabetes mellitus is a common and serious problem that is rapidly emerging as a global health care issue that may reach pandemic levels by 2030, with the most noticeable increase occurring in developing countries.¹ Although the prevalence of type-1 and type-2 diabetes mellitus is increasing worldwide, the prevalence of type-2 diabetes is rising much more rapidly because of increasing obesity and reduced activity levels as countries become more industrialized.² According to recent estimates, the prevalence of diabetes will increase to 7.1% by year 2025, affecting some 380 million people worldwide.³ Pakistan was at number 8 in the world in 1995 with 4.3 million people affected by diabetes mellitus and it is estimated that Pakistan will be at number 4 with 14.5 million people with this disease by the year 2025.⁴ It was found that increased age, the number of complications and longer duration of disease significantly increase the burden of cost on society.⁵

People with diabetes are at higher risk for a number of serious health problems including cardiovascular disease (CVD), premature death, blindness, kidney failure, amputations, fractures, depression, and cognitive decline.⁶ CVD is the most common complication associated with diabetes. The worldwide epidemic of diabetes is increasing the burden of cardiovascular diseases, the leading cause of death among the person with diabetes.⁷ Diabetes and coronary artery disease often appear as

the two sides of the same coin; on one side diabetes has been rated as an equivalent of coronary artery disease. According to Global registry for acute coronary events, approximately one in four patients presented with acute coronary syndrome had history of diabetes.⁸ A study in Pakistani province Sindh, observed that one out of every three patients with acute myocardial infarction had either diabetes or elevated levels of random blood glucose.⁹ In acute coronary syndrome, diabetes confers a significant adverse prognosis with mortality at 30 days and at one year, significantly higher than patients without diabetes.¹⁰ Nephropathy may already be established at presentation in type-2 patients and is a common long term complication for those with type-1 diabetes. Because endothelial cell dysfunction and inflammation are key contributors to the development of vascular complications in diabetes mellitus,¹¹ so nephropathy leading to albuminuria, and macro-vascular complications of diabetes mellitus are related to each other. Albuminuria is common in diabetics and marks out those likely to develop macro-vascular diseases.^{12,13}

Because of the importance of diabetes mellitus and macro-vascular complications resulting thereafter, we need to study factors linking to macro-vascular complications in diabetes, so that impending serious vascular problems in this disease might be guessed by these factors, which in the context of public health will help the care givers and the policy makers to suggest and focus

on meaningful interventions. Aggressive management including good glycemic control, blood pressure control, aspirin, ACE inhibitors and statins¹⁶, may enable us to decrease toll of morbidity and mortality in targeted population, which is not always possible in all patients in our limited resources, thus producing burden of vascular disability on our nation. In this context, current study is going to correlate albuminuria detected on heating method in diabetics with subsequent macro-vascular events

MATERIAL AND METHODS

The descriptive study was conducted in departments of cardiology and medicine of Ayub Medical College, Abbottabad from December 2010 to May 2011. A total of 88 diabetic patients with macro-vascular complications were enrolled in the study by consecutive/non-probability sampling. Sample size was calculated using the WHO software for sample size calculation in health studies, with the assumptions: Proportion of diabetics with albuminuria=35%¹³, confidence level=95% and specified absolute precision=10%

All the diabetic patients admitted with myocardial infarction (MI) or stroke of either gender above 20 years of age were included in the study. Patients with urinary tract infection, smokers and patients of stroke with valvular heart diseases or atrial fibrillation were excluded from the study. Informed consent of patient or patient’s attendant was taken after explaining them the study protocol. Detailed history was taken including symptoms of hyperglycemia, type of diabetes, treatment taken, compliance with treatment, years after diagnosis of diabetes and history regarding exclusion and inclusion criteria for study. The patients were then examined especially focusing on cardiovascular and neurological examination. Investigations of patients were thoroughly followed from patient’s record, especially venous blood glucose, CT/MRI and Troponin-T levels which are performed as a routine for patients admitted with myocardial infarction or stroke.

Two urine specimens of selected patients fulfilling criteria for study were collected. One was examined for the albumins by dipstick method and infection, and second was taken to chemical pathology laboratory, where it was subjected to heating method of albumin detection in a test tube. In this method test tube filled with urine was heated at top with little inclination till boiling. Then few drops of full strength nitric acid were added and any visible coagulum left at surface was regarded as albumin in urine sample. Data was collected using predesigned pro forma and analysed by SPSS-14.0.

RESULTS

A total of 88 patients with diabetes mellitus and macrovascular complications were inducted in this study. There were 49 (55.7%) male and 39 (44.3%) female patients. The mean age for the participants of study was 47.12±7.58 years (range 36-68 years). Out of total 88 patients, 14 (15.9%) patients had type-1 diabetes while remaining 74 (84.1%) were non-insulin dependent type-2 diabetic patients. 7 males and 7 female diabetic patients with macro-vascular complications had type-1 diabetes mellitus. Out of total 88 patients 70 patients (79.5%) were taking some form of treatment for diabetes while 18 patients (20.5%) were getting no treatment at all.

Mean fasting glucose of the patients was 12.23 mmol/l, while mean random sugar was 17.73 mmol/l. Mean glucose values indicate poor control of diabetes even in the group of patients taking some form of treatment for diabetes. 14 patients (15.9%) were recorded having haemorrhagic cerebrovascular accident (CVA), 22 patients (25%) with ischaemic CVA, while 52 patients with troponin-T positive myocardial infarction as summarized in table-1 and 2.

Twenty six out of 29 male patients with MI had urinary albumin positive on heating method (89.65%) while 22 out of 23 female diabetic patients with MI (95.65%) had positive result for urinary albumin. 18 out of 20 male patients (90%) with stroke had positive albumin in urine, in which haemorrhagic CVA patients were 7 with 6 patients (85.7%) having albumin in urine. 12 out of 13 male diabetics with ischaemic stroke had albumin in their urine (92.3%). On the other hand 15 out of 16 female diabetic patients with stroke got positive results for urinary albumin (93.75%), in which haemorrhagic stroke patients were 7, out of which 6 patients were positive for urinary albumin (85.7%), while all 9 female diabetic patients with ischaemic stroke had albumin in their urine as detected on heating method.

Table-1: Various macro-vascular complications according to type of diabetes.

Type of Diabetes	Complication			Total
	CVA (H) Number of patients	CVA (I) Number of patients	MI Number of patients	
Type-1	4	2	8	14
Type-2	10	20	44	74
Total	14	22	52	88

Table-2: Comparison of albuminuria in various macro-vascular complications of diabetes

Urinary Albumin	Complication		
	CVA (H) Number of patients	CVA (I) Number of patients	MI Number of patient
Albumin Positive	12	21	48
Albumin Negative	2	1	4
Total	14	22	52

DISCUSSION

Various studies have shown that albuminuria is an important risk factor for arteriosclerosis, ischaemic heart disease and other vascular diseases in diabetics.¹³ Diabetic nephropathy is found to be significantly associated with diabetic retinopathy and coronary artery disease and a few studies have also shown an association between diabetic nephropathy and neuropathy, and peripheral vascular disease.¹⁴

Because endothelial cell dysfunction and inflammation are key contributors to the development of vascular complications in diabetes mellitus,¹¹ so nephropathy leading to albuminuria and macro-vascular complications of diabetes mellitus are related to each other. Albuminuria is common in diabetics (about 35%)¹³ and marks out those likely to develop macro-vascular diseases.¹² Studies concluded that close association between albuminuria and other macro-vascular complications exists in patients of Indian sub-continent also.¹⁴

Although diabetes is more common in older individuals, the incidence is increasing at a dramatic rate in all races and age groups especially in young adults and macro-vascular disease is the most common cause of death in this population (>75%).¹⁵ Prevalence of cerebro-vascular disease in diabetics is 7% having 2–3 times increased risk of fatal stroke as compared to general population, while coronary artery involvement is in 18% having 3–5 times increased risk of fatal heart disease and intermittent claudications are in 4.5% having 15 times increased risk of amputation as compared to general population.¹⁵

It is an area of active research as to what is the role of detecting albuminuria by simple or sophisticated methods in finding out diabetic individuals at highest risk of impending macro-vascular complications. Although all diabetic patients have higher risk of macro-vascular complications than general population, but if we find some way of selecting sub group of patients who are at highest risk, then we can focus our special attention in these patients in terms of tight glycaemic control, blood pressure control, aspirin, ACE inhibitors and statins, and thus enabling us to decrease toll of morbidity and mortality in targeted population.² This becomes more important in our country Pakistan, where we are facing limitations like lack of education, limited resources and other problems which increases a burden of macro-vascular complications in our diabetic population. Albuminuria as detected by simple heating method in laboratory is a ray of hope in this regard, and can be considered as a prelude for impending macro-vascular complications of diabetes. So patients with albuminuria are candidates of special attention in preventive strategy of macro-vascular complications in diabetics.

Many studies regarding association of albuminuria with macro-vascular complications of diabetes mellitus are published recently. In their result albuminuria is found to be independent predictor of macro-vascular complications.¹⁶ It was associated with two-fold increased risk of cardiovascular events and 18.3 times higher standardized mortality ratio in large cohort studies.^{17,18} Overview of 11 cohort studies suggested overall odds ratio for death in albuminuria positive patients as 2.4 (95% confidence interval, 1.8–3.1) with cardiac mortality odds as 2 (95% confidence interval, 1.4–2.7) with no evidence of reporting bias.¹⁹ In seven studies comprising 46,638 participants with 1,479 stroke events, albuminuria was strongly linked to stroke risk, but it is unclear whether stroke incidence varies by level of albuminuria, and needs further evaluation.^{16,20}

CONCLUSION

Albuminuria is significantly higher in diabetic patients with macro-vascular complications. Therefore we can regard albuminuria in diabetic patients as a prelude for impending macro-vascular complications of diabetes. It is however worth mentioning that routine dipstick examination is not a good test for detecting albuminuria in diabetic patients as only 46 percent of patients had positive result for albumin in their urine on dipstick in contrast to heating method of albumin detection which detected 92% diabetic patients with macro-vascular complications having positive albumin in their urine.

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