

Clinical Applications of Microalbuminuria

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ABSTRACT

Microalbuminuria is a marker for generalized vascular dysfunction. Persistent microalbuminuria indicates a high probability of damage to the glomerular filtration capacity of the kidney and is of great diagnostic relevance. Albuminuria has also been shown more recently to be a predictor of cardiovascular outcomes. Emerging data that reduces albuminuria leads to reduced risk of adverse renal and cardiovascular events, and steps should be taken to suppress albuminuria to prevent future renal and cardiovascular adverse events. This review discusses the measurement of albuminuria and summarizes the current literature on the association between albuminuria and adverse cardiovascular and renal outcomes in type 2 diabetes and hypertension.

Key words: Hypertension, Diabetes mellitus, Steno hypothesis, Diabetic nephropathy

INTRODUCTION

Daily excretion of albumin is generally in the range of 5-10 mg, and the urine albumin: creatinine ratio is 0-29 mg albumin / g of creatinine. Microalbuminuria is defined as an abnormal increase in albumin excretion rate within the range of 30-299 mg of albumin / g of creatinine. The term microalbuminuria refers explicitly to an abnormal albumin excretion rate, not the presence of an albumin molecule. Microalbuminuria was first coined by (Mogensen 1984) and others as 30–300 mg urinary albumin excretion per 24 h. The term ‘microalbuminuria’ is a relative misleading term; it implies ‘small size’ but refers to the presence of a relatively ‘small quantity’ of protein in the urine(Viberti et al., 1982). Microalbuminuria is defined as a urine albumin excretion between 20 and 200 µg/min or 30 to 300 mg in overnight or 24-h collection.

Albumin is expressed as a ratio to creatinine is used to detect an abnormal amount of albumin in 24 hours urine collection. It is also recommended by the National Kidney Foundation, The American Diabetes Association and the National Institutes of Health.

Since microalbuminuria is an important adverse predictor of various diseases and is the first detectable sign of early ailments, this study reviews the pathophysiology of microalbuminuria. In addition, it discusses the measurement of albuminuria and the association between albuminuria and adverse cardiovascular and renal outcomes in type 2 diabetes and hypertension.

Detection and measurement of Microalbuminuria

- 1. A urine dipstick test** is a test in which a test strip turns a different color based on the amount of albumin in the sample. A dipstick test does not provide an exact measurement of albumin.
- 2. A 24-hour urine sample** requires collecting all of your urine for a full day. The laboratory then measures the total amount of albumin in that complete sample. Therefore, a 24-hour urine sample provides an albumin measurement that is typically listed as milligrams per 24 hours (mg/24 hours).
- 3. An albumin-to-creatinine ratio test** measures albumin and creatinine in a one-time sample, also known as a spot urine sample. Creatinine is a chemical by-product of regular muscle activity, and it is generally removed from the body in urine. Total daily creatinine production is relatively consistent, so an albumin-to-creatinine ratio test is a way to estimate your total daily urine albumin level without having to do a full 24-hour urine sample. An albumin-to-creatinine ratio test is reported in milligrams of albumin per gram of creatine

(mg/g) found in one deci liter of urine. This may also be listed in international units, which are measured in milligrams per millimole (mg/mmol) (Seema Basi et al., 2008)

Microalbuminuria - significance

Microalbuminuria is an independent predictor of progressive renal disease and cardiovascular diabetes and hypertension. Therefore, screening for microalbuminuria in children seems highly relevant in the paediatric population to detect and prevent cardiovascular disease. In the last few years, several studies have pointed out the role of microalbuminuria as a predictor of cardiovascular morbidity and mortality.

The 5-year follow-up study conducted in 50- to 75-year-old subjects tested the hypothesis that microalbuminuria may reflect generalized atherosclerosis. It was observed that both microalbuminuria (albumin-to-creatinine ratio >2 mg/mmol) and peripheral arterial disease were associated with a fourfold increase in cardiovascular mortality, which was more marked in hypertensive subjects than in normotensive subjects.

What Causes Microalbuminuria?

Microalbuminuria is caused by kidney damage. Some medical conditions that can lead to kidney damage include:

- High blood pressure
- Type I and type II diabetes
- Obesity and metabolic syndrome
- Genetically inherited kidney diseases

Detection of Albuminuria in Various Disease

Evidences Showed, microalbuminuria was associated and clustered with other widely known CV risk factors (age, diabetes, hypertension, LVH, overweight, metabolic syndrome, clustered with other widely known CV risk factors (age, diabetes, hypertension, LVH, overweight, metabolic syndrome, etc.) that could explain the increased CV risk.

1. Microalbuminuria and Cardiovascular Risk

Mogensen (1) wrote a seminal paper in 1984, describing the importance of microalbuminuria as a renal risk factor and cardiovascular risk factor in patients with diabetes. For patients with hypertension or diabetes mellitus, it is also a marker for significantly increased cardiovascular risk. Indeed, recent studies have established a relationship between albuminuria and cardiovascular risk regardless of diabetes. The association of microalbuminuria with elevated blood pressure (BP) is consistent and independent. An increased urinary albumin excretion rate has also been linked to lipid

abnormalities, reduced insulin sensitivity, impaired endothelial function, peripheral vascular disease, and a prothrombotic state (Borch-Johnsen et al., 1999). Thus, microalbuminuria is a marker of generalized vascular dysfunction. (Jager et al., 1999)

2. Microalbuminuria and Diabetes mellitus

An analysis reveals generalised endothelial dysfunction as a common denominator in microalbuminuria in both the general and diabetic populations. In 1989, this observation led to the hypothesis that a common process underlies both microalbuminuria and generalised endothelial dysfunction in diabetes. This process was suggested to be the dysregulation of enzymes involved in extracellular matrix metabolism, the ‘Steno hypothesis’ (Romundstad et al., 2003), diabetes exerts its effects on glomerular permeability in the initiating stages of diabetic nephropathy, i.e., at or before the appearance of microalbuminuria. These early changes establish the milieu in which the more advanced changes of overt diabetic nephropathy develop. Defining the mechanistic links from biochemical derangements to the appearance of increased urinary albumin highlights key elements in the pathophysiological pathway of developing diabetic nephropathy and micro-and macrovascular disease elsewhere. (Gerstein HC et al., 2001)

The insulin resistance syndrome describes the clustering of disorders, the underlying pathology of which is related to insulin resistance and endothelial dysfunction. Microalbuminuria is associated with several disturbances found in the insulin resistance syndrome, including endothelial dysfunction and obesity, in addition to type 2 diabetes. Proinflammatory cytokines produced by visceral adipocytes (adipokines) have recently emerged as important mediators of the increased cardiovascular risk associated with insulin resistance syndrome. These adipokines represent a possible link from insulin resistance and obesity to microalbuminuria in the non-diabetic population. (Knobl et al., 2001)

Thus, in the diabetic and the general population, the risk factors for developing microalbuminuria can be grouped into those associated with vascular disease, including endothelial dysfunction, inflammation, and insulin resistance. (Deckert et al., 1989). This implies that microalbuminuria may also, at least in these situations, result from endothelial dysfunction (Schalkwijk, Stehouwer 2005)

Microalbuminuria and hypertension

Although microalbuminuria was initially diagnosed in diabetic patients, the exact definition was used for other clinical conditions including hypertension (Chaturvedi et al., 2001). Microalbuminuria is more frequent in subjects with moderate to severe

hypertension and less prevalent in subjects with mild, uncomplicated hypertension in whom the albumin excretion rate level may be even lower than that in normotensive subjects (Rosa, Palatini et al., 2001). Many factors may affect the albumin excretion rate and influence the prevalence of microalbuminuria. Exercise is known to increase the albumin excretion rate level in normal individuals. . Obviously, urinary tract infections can affect albumin excretion rate level. When a symptomatic infection is present, evaluation of albumin excretion should be postponed until the infection is effectively treated. Heart failure and acute illnesses with fever are other potential sources of increased albumin excretion rate level, even though this is not always to a pronounced extent (Jones et al., 2002). Individuals with essential hypertension who develop microalbuminuria have a higher incidence of biochemical disturbances, implying that hypertension per se may not be the cause of microalbuminuria, but, rather, these other derangements (Bianchi et al., 1999). Microalbuminuria is strongly associated with vascular disease in hypertensive patients, suggesting a marker of vascular and endothelial damage in this condition (Jensen et al., 2000).

Microalbuminuria and Diabetic nephropathy

Diabetic nephropathy is the leading cause of chronic kidney disease. Diabetic nephropathy has been classically defined by the presence of proteinuria >0.5 g/24 h. This stage has been referred to as overt nephropathy, clinical nephropathy, proteinuria, or macroalbuminuria. Diabetes causes notable changes in kidney structure (Mauer et al., 1981). Classic glomerulosclerosis is characterized by increased glomerular basement membrane width, diffuse mesangial sclerosis, hyalinosis, microaneurysm, and hyaline arteriosclerosis. Tubular and interstitial changes are also present (Fioretto et al., 1996). Micro- and macroalbuminuric patients with type 2 diabetes have more structural heterogeneity than patients with type 1 diabetes. After the diagnosis of micro- or macroalbuminuria is confirmed, patients should undergo a complete evaluation, including a work-up for other etiologies and an assessment of renal function and the presence of other comorbid associations. Patients with diabetic nephropathy, due to their high cardiovascular risk, should be routinely evaluated for the presence of coronary heart disease, independently of the presence of cardiac symptoms (Osterby et al., 1993).

Conclusion

The associations between microalbuminuria, cardiovascular disease and progressive renal impairment are well described. In summary, the various avenues of study of diabetic microalbuminuria reviewed converge on the glomerular endothelium. This is the site of the initial damage that leads to the development of microalbuminuria in diabetes. Evidences stated that reduction of albuminuria leads to improvement in the risk profiles of these patients. Early detection of diabetic nephropathy, adopting multifactorial interventions targeting the main risk factors (hyperglycemia, hypertension, dyslipidemia, and smoking), and using agents with a renoprotective effect (ACE inhibitors and ARBs) do indeed reduce the progression of renal disease. Treatment of hypertension is a priority. Attention to these procedures will also ensure the reduction of cardiovascular mortality.

Author contribution

Jayamathi Govindaraj, Keerthidaa Govindaraj conceived of the presented idea S.Bhuminathan , Kesavaram Padmavathy ,Vidyarekha U, Kannan N and Yogarajan R encouraged and supervised the findings of this work. All authors discussed the results and contributed to the final manuscript.

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Study significance

This review discusses the measurement of albuminuria and summarizes the current literature on the association between albuminuria and adverse cardiovascular and renal outcomes in type 2 diabetes and hypertension.

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