Clinical applications of Micro albuminuria

Abstract

Microalbuminuria is a marker for generalized vascular dysfunction.Persistant microalbuminuria indicates high probability of damage to 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 reduction of albuminuria leads to reduced risk of adverse renal and cardiovascular events but also steps should be taken tosuppress albuminuria to prevent futurerenal and cardiovascular adverse events.This review discusses the measurement ofalbuminuria and summarizes the currentliterature on the association between albuminuriaand adverse cardiovascularand renal outcomes in type 2 diabetes andhypertension.

Key words: Hyper tension, Diabetes mellitus, Steno hypothesis, Diabetic nephropathy

Introduction

Normally, daily excretion of albumin is in the range of 5-10 mg and the urine albumin : creatinine ration is in the range of 0-29 mg albumin / g of creatinine. Microalbuminuria is defined as abnormal increase in albumin excretion rate within the range of 30-299 mg of albumin / g of creatinine. The term microalbuminuria specifically refers to an abnormal albumin excretion rate not the presence of albumin molecule. Microalbuminuria was first coined byMogensen (1) 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 actually refers to the presence of a relatively ‘small quantity’ of protein in the urine(2). Microalbuminuria is defined as a urine albumin excretion between 20 and 200 μg/min or 30 to 300 mg in an 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 AmericanDiabetes 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 review the pathophysiology of microalbuminuria

and 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. 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 both albumin and creatinine in a one-time sample, also known as a spot urine sample. Creatinine is a chemical byproduct of normal muscle activity, and it is normally 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 deciliter of urine. This may also be listed in international units, which are measured in milligrams per millimole (mg/mmol)(3).

Microalbuminuria -significance

Microalbuniuira is an independent predictor of progressive renal disease and cardiovascular diabetes and hypertension. In children, screening for microalbuminuria seems highly relevant in the pediatric 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 (4).

The hypothesis that microalbuminuria may reflect generalized atherosclerosis was tested in the 5-year follow-up period study conducted in 50- to 75-year-old subjects. It was observed that both microalbuminuria (albumin-to-creatinine ratio>2 mg/mmol) and peripheral arterial diseasewere associated with a fourfold increase in cardiovascular mortality, which was more marked in hypertensive subjects than in normotensive subjects (5 &6).

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
- Genetic inherited kidney diseases

Detection of Albuminuria in Various Disease

Evidences Showed (7), 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 Cardio vascular Risk

Mogensen (1) wrote a seminal paper in 1984, describing the importance of microalbuminuria not only as arenalrisk factor but also as a cardio vascular risk factor in patients with diabetes. For patients with hypertension or diabetes mellitus, it is also a marker for greatly increased cardiovascular risk. Indeed, recent studies have established a relationship between albuminuria and cardiovascular risk regardless of the presence of diabetes. The association of microalbuminuria with elevated blood pressure (BP) is consistent and independent, and 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(8). Thus, microalbuminuria is a marker of generalized vascular dysfunction.

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 metabolism of extracellular matrix, the ‘Steno hypothesis’(9),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 the development of both diabetic nephropathy and micro- and macrovascular disease elsewhere.

The insulin resistance syndrome describes a clustering of disorders, the underlying pathology of which is thought to be related to insulin resistance and/or endothelial dysfunction. Microalbuminuria is associated with several of the 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 the insulin resistance syndrome. These adipokines represent a possible link from insulin resistance and obesity to microalbuminuria in the non-diabetic population. (10)

Thus, in the diabetic as well as in the general population the risk factors for the development of microalbuminuria can be grouped into those associated with vascular disease, including endothelial dysfunction, inflammation and insulin resistance. This implies that microalbuminuria may also, at least in these situations, result from endothelial dysfunction. (11)

Microalbuminuria and hypertension

Although microalbuminuria was initially diagnosed in diabetic patients, the same definition was subsequently used for other clinical conditions including hypertension. (12). Obviously, 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 thatin normotensive subjects (13). Many factors may affect albumin excretion rate and influence the prevalence of microalbuminuria. Exercise is known to increase albumin excretion rate level in normal individuals. . Obviously, urinary tract infections can affect albumin excretion rate level, and 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(12). 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 additional derangements(14). Microalbuminuria is strongly associated with vascular disease in hypertensive patients, suggesting that it is a marker of vascular and/or endothelial damage in this condition(15).

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 unique changes in kidney structure(16). 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. 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(17& 18)

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, adoption of multifactorial interventions targeting the main risk factors (hyperglycemia, hypertension, dyslipidemia, and smoking), and use of agents with a renoprotective effect (ACE inhibitors and/or 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.

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