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Microalbuminuria: A Urinary Biomarker of Diabetic Kidney Disease

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Diabetes Mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia and disorders of carbohydrate, protein and lipid metabolism.[1] It is expected that by the year 2030, about 552 million people globally will be affected from diabetes mellitus.[2] If not well controlled, diabetes mellitus leads to both microvascular and macrovascular complications.[2] Diabetic mellitus is the most common cause of diabetes nephropathy that has a momentous impact on quality of life and survival of the patient.[1] It is estimated that about 40 % of type I and type II diabetes mellitus develop diabetic kidney disease.[2] If not timely diagnosed and properly treated, diabetic nephropathy eventually leads to End stage renal disease that requires dialysis or renal transplantation. Multiple serum and urinary biomarkers are used to diagnose diabetic nephropathy before it is clinically evident.[2] Urinary microalbumin has been used as a clinical biomarker of diabetic kidney disease since 1982.[4] It is used to screen both type I and type II diabetes mellitus.[5] Microalbuminuria results when albumin crosses glomerular filtration barrier due to ultrastructural changes in endothelial glycocalyx.[6] Microalbuminuria also represents a marker of systemic endothelial dysfunction with increased risk of cardiovascular and cerebral insults in patients with diabetes mellitus.[7]

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In addition to glomerular injury, newer biomarkers of tubular, vascular, inflammation, podocytes and oxidative stress have been verified in some patients that detect diabetic nephropathy much earlier than microalbuminuria.[3] Usefulness of these biomarkers is still debatable in research due to limited studies performed and requires further validation.[3] Microalbuminuria even disputed as biomarker of early diabetic nephropathy, is still considered as an important screening test to detect glomerular and tubular injury in diabetic population.[3] American Diabetes Association guidelines recommend initial assessment of urinary albumin excretion in type I diabetes mellitus who have had diabetes for at least five years and in all patients with type II diabetes mellitus at the time of presentation and during pregnancy.[8] All diabetic patients with negative screening test for microalbuminuria should be assessed for kidney functions on annual basis.[9]

Microalbuminuria (although a misnomer term) is detection of small quantity of albumin (and not small-size albumin) in the urine i.e. 30-300 mg/24 hours or 20 to 200 µg/min in the absence of clinical proteinurea as measured by standard analytical methods.[7] More appropriate term for microalbuminuria is paucialbuminuria or albumin excretion rate.[10]

Normal urinary albumin excretion is less than 30 mg/24 hours (20ug/min). This small amount is not detectable by

routine dipstick method of urine analysis.[11] Spot urinary albumin to creatinine ratio is more useful indicator and is comparable to 24 hours urine collections. Measurement of albumin to creatinine ratio (ACR) eliminates variations in urine flow rate on a spot urine specimen.[11]

Albumin to creatinine ratio of 30 to 300 mg/g of creatinine suggests that albumin excretion is between 30 and 300 mg/24 hours and, therefore, microalbuminuria is present. ACR value of ≥300 mg/g or ≥300 mg/24 hours are indicative of macroalbuminuria or clinical proteinurea. This classification system requires that at least two of three specimens fall within the microalbuminuric or macroalbuminuric range over a 3 to 6 months period. Factors that influence urinary albumin excretion must be taken into consideration. These factors include high grade fever, sever infection exercise within 24 hours, congestive cardiac failure, severe hyperglycemia and high blood pressure.[9]

It is recommended that urinary protein may first be tested by routine dipstick method on spot urine sample to rule out overt proteinuria. This practice avoids loss of laboratory resources and manages work load. When urinary protein by dipstick is negative, only then spot urine sample should be tested for microalbuminuria or albumin to creatinine ratio.

Microalbuminuria has a variable progression. It can revert to normal, progress to macroalbuminuria or can remain static. Interventions like good glycemic control, use of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers for control of blood pressure reduce microalbuminuria and prevent further loss of renal functions.[3]

Concomitant analysis of several urinary biomarkers along with microalbuminuria can diagnose early diabetic nephropathy. However, discovery of a new and ideal urinary biomarker that is more sensitive and specific than microalbuminuria is still awaited. Early detection of diabetic kidney disease with such newer biomarkers in future will minimize renal complications of diabetes mellitus by appropriate and timely interventions.[3]

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