IS MICROALBUMINURIA AN EARLY MARKER OF DIABETIC RENAL DISEASE?

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Involvement of kidneys as a late complication of Diabetes Mellitus is considered to be the most serious element of the diabetic triopathy — retinopathy — neuropathy and nephropathy. It is the only one which influences the life expectancy of the diabetic as it has a progressive course. How can diabetic nephropathy be identified at an early stage? What are the early markers to be searched? Can its progress be arrested, slowed down or reversed? All these questions have introduced new concepts and ideas in the field of nephrology and diabetology. 'Microalbuminuria' has been claimed to be a very useful parameter[1] for tracing and tracking the very early cases of diabetic nephropathy especially in the insulin dependent diabetics. It is an established fact that, in normal individuals, very small quantities of plasma albumin are filtered by the renal glomeruli of which 95 to 98 percent is reabsorbed in the proximal tubules. Thus the urinary excretion of albumin does not exceed 15 micrograms per minute or 20mg in 24 hours. Proteinuria has been defined as a total urinary protein excretion of 500 mg per 24 hours or more. This is equivalent to a urinary albumin excretion rate of 200 micrograms per minute. Urinary albumin excretion Ehat is higher than normal but less than that associated with proteinuria or that between 15 and 250 micrograms per minute is labelled as "Microalbuminuria". It is detectable only by special sensitive assay methods[2,3]. Proteinuria and renal disease have been linked with diabetes mellitus since a centur4y. It was first described by Kimmeistiel and Wilson in 1936[4] as the nodular glomerular lesion or intercapillary glomerular hyalinoscierosis. Since then intensive studies alongwith the use of electron microscopy has enabled detailed and exact description of the changes appearing in the kidney tissue due to diabetes. Fibrinoid changes in the walls of both afferent and efferent glomerular arterioles with thickening of the capillary basement membrane are related to diabetes mellitus. As the process progresses more and more glomeruli become hyalinised and eventually functionless[5], and the downhill course leads to end-stage renal failure[6]. The renal changes associated with diabetes mellitus have been described as hyperfiltration, nephromegaly and microalbuminuria. The abnormally increased glomerular filtration rate is encountered in 40 percent patients in the initial months or years after diagnosis of diabetes[7]. This is interlinked with nephromegaly and an increased renal volume upto 60 percent[8]. Microalbuminuria is a fairly new concept regarded as an early change of renal function and structure predicting the subsequent development of advanced disease of the kidney in the diabetics[9]. The pathophysiology of microalbuminuria is still debatable. It has been ascribed to haemodynamic alterations in the kidneys[10], or in the glomerular filter[11]. The transcapillary escape rate of albumin is increased in diabetics with incipient nephropathy and these two factors have been attributed to be the causative mechanisms. Other theories indicate impaired properties of permeability of the glomerular basement membrane in these cases[12]. A rise in the arterial pressure which may still be within the normal range has been noted in diabetics with microalbuminuria[13]. When does this gradual rise of blood pressure begin? Observations have shown both the increasing blood pressure and U aib V (albumin excretion rate) to be closely time related. It has also been proved that the diabetic state may directly affect the blood pressure which is higher during poor metabolic control[14]. Therapeutic intervention in cases of microalbuminuria aims at preventing or delaying overt nephropathy. Metabolic control has its due importance in the prevention and progression of diabetic micro and macro angiopathy. Most studies have documented that the rate of progression of microalbuminuria is delayed by an improved metabolic control[15]. This was also supported by the correlation between

HbA1c and the annual change of U aib V and the rate of decline of GFR in the studies conducted[16]. Antihypertensive therapy instituted in patients with incipient nephropathy or microalbuminuria has resulted in an improved renal status. The GFR increased and a reversal in the microalbuminuria was noted in the follow up studies upto ten years[17]. Diuretics, beta blockers and other conventional antihypertensive therapies have an important role in stabilizing blood pressure and thus improving the kidney function. Angiotensin converting enzyme inhibitors seem to have taken a lead in this field. They have proved more beneficial because they simultaneously reduce glomerular hypertension[18]. Studies have also been conducted to see the effects of ACE inhibitors on normotensive insulin dependent diabetics with microalbuminuria. The results obtained were a reduction in systemic blood pressure, U aib V, fractional albumin clearance and total renal vascular resistance. This again indicated a decline in the intraglomerular pressure[19]. ACE inhibitors combined with diuretics especially in diabetics with a low supine serum angiotensin 2 level have proved very successful as they excrete the excess sodium without reactivation of the renin-angiotensin system. Protein restriction is known to modify renal haemodynamics thus proving beneficial in diabetics with renal disease[20]. Short term studies of three weeks duration with protein restriction on insulin dependent diabetics with microalbuminuria indicated a reduction in UalbV and fractional albumin clearance[21]. Other therapeutic interventions are still being studied and need time to prove their efficacy. Prostaglandin inhibitors have been found to exert a favourable effect on the functional abnormalities of diabetic nephropathy. Indomethacin causes a short term reduction in glomerular hyperfiltration and albuminuria in insulin dependent diabetics. Inhibition of aldose reductase by sorbinil has been studied in animals leading to regression of the glomerulopathy[22]. To place microalbuminuria as a prognostic factor for renal complications in diabetes mellitus is still a debatable topic. Much work is being done on the subject but it is an accepted fact that microalbuminuria is a sign denoting the presence of established lesions in the kidneys. Besides, all available evidence leads to the conclusion that improved metabolic control and antihypertensive therapy does either arrest or delay the late complications of diabetes especially the kidney related ones. A close monitoring of diabetic patients with microalbuminuria to keep their glycaemic control and blood pressure in optimal range will prove beneficial in the long run. Further long term studies on the subject are awaited which will provide a new horizon for renal complications of diabetes mellitus.

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