EVALUATION OF URINARY TUBULAR ENZYMES AS SCREENING MARKERS OF RENAL DYSFUNCTION IN PATIENTS SUFFERING FROM DIABETES MELLITUS TYPE 2

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Diabetes mellitus is a global disorder and complications resulting from the disease are the third leading cause of death in the world. A survey by the National Diabetes Data Group estimates the prevalence of diabetes in the world population at 6.6%. One of the principle complications of diabetes mellitus is diabetic nephropathy and renal function tests are important indicators in diabetic patients needed to identify the early structural and functional changes in diabetic nephropathy. Diabetes mellitus type 2 patients show elevated levels of albumin in urine and assessment of renal injury based on the concentrations of blood urea nitrogen (BUN), serum creatinine (S.Cr) or urinary micro protein (U.MP) that are commonly used are usually insensitive since these parameters could be within normal ranges despite considerable impairment of the renal function because of the great reserve capacity of the kidney. More sensitive urinary biomarkers, which could be used to detect nephrotoxicity at early stages on various parts of the nephron, are being investigated. Animal studies have identified enzymes as potential urinary biomarkers of renal injury. These biomarkers include the high molecular weight albumin for evaluating glomerular integrity, the brush border enzymes alkaline phosphatase (U.ALP) and gamma glutamyl transferase (U.γ-GT), lysosomal enzyme N-acetyl-β-D-glucosaminidase (U.NAG), and cytoplasmic enzyme lactate dehydrogenase (U.LDH) for indicating proximal tubular injury. The present study investigated early signs of renal injury due to diabetes mellitus type 2 by measuring urinary indicators of nephrotoxicity. The study subjects comprised 251 patients with diabetes mellitus type 2 (mean age 54.2yrs) and 73 healthy normal individuals recruited as control group (mean age 40.9 yrs). The diabetic group was further subdivided into those with normoproteinuria, microproteinuria and diabetics with renal failure. Glomerular function was studied by determining the urinary levels of micro protein (U.MP), serum urea and creatinine while proximal tubular structural integrity was studied by determining the activities of the enzymes U.ALP, U.NAG, U.γ-GT, and U.LDH. Compared with normal healthy individuals, diabetic patients with normoproteinuria excreted significantly high levels of U.ALP, U.LDH, U.γ-GT, and U.NAG (p<0.05). Patients with renal impairment excreted high levels of the enzymes and urinary micro protein compared to healthy individuals and diabetic patients without renal failure. In conclusion, the present study confirms that diabetes mellitus leads to nephrotoxicity; that urinary excretion of U.ALP, U.LDH, U.γ-GT, and U.NAG could be useful biomarkers for proximal tubular injury. These results suggest that site-specific urinary biochemical markers provide valuable information about early renal proximal tubular insult that ultimately may precede glomerular permeability in subjects with diabetes mellitus.