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Comparative study of novel urinary biomarkers in non-hypertensive early diabetic (include pre-diabetes) and late diabetic nephropathy

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Background: Novel urinary biomarkers (UBM) which include angiotensinogen (AGT), cystatin C (Cys C), interleukin-18 (IL-18) and neutrophil gelatinase associated lipocalin (NGAL) estimation may detect nephropathy even in hyper-filtration stage, understand pathophysiology thereby preventing progression. Although conventional urine micro albumin testing is the gold standard for detecting early diabetic nephropathy (DN), identifying sensitive biomarkers that can predict the course of MA will facilitate early diagnosis and prognosis and guide interventional strategies. However, nephropathy in early diabetic is not clear. We define pre-diabetics and diabetics of one year duration as early diabetic.

Aim: The aim of this work was to study the comparison of novel UBM in non-hypertensive, early diabetic and late diabetic nephropathy.

Methods: All patients attending OPD were screened as per their past history, clinical records to define pre-diabetic and diabetic state. They underwent detailed clinical examination such as measurement of blood pressure, body weight, height and investigations which include fasting and post prandial blood sugar, HbA1C, routine urine examination by Multistix, albumin creatinine ratio (ACR) and serum creatinine for calculation of estimated glomerular filtration rate (e-GFR). Considering inclusion and exclusion criteria, the same investigations has been repeated after three months. Thereafter, study subjects were included. The ACR and e-GFR were repeated at sixth and 12th month to see the progression. At sixth month, all the UBM's (NGAL, AGT, IL-18, Cys C) of early diabetics were estimated and compared with that of diabetics.

Results: A total of 953 patients were screened. Of them, 44 (4.6%) were pre-diabetic, 133 (13.96%) were early-diabetic, and 708 (74.29%) were diabetic. After exclusion, 158 met our inclusion criteria, and 47 were categorized as early diabetics (these included pre-diabetes) and 111 had diabetes. Average age of early diabetic and late diabetics was 46.6±9 and 50.7±9.7 respectively. At the end of the sixth month, there was no significant difference of UBM in early and late diabetic nephropathy. However, all the UBM values of normal individuals (from published studies) were found to be elevated significantly {(mean difference, standard error, p value). NGAL, ATN, IL-18 and cystatin C of early diabetics were (-23.9, 7.52, 0.0007), (-193.55, 27.35, 0.0000), (-16.69, 4.53, 0.0002) and (-18.82, 1.832, 0.000) respectively} when compared with the diabetic patients. At one year, it was found that the average GFR value decreased to normal from the hyper filtration state (GFR □120 ml) and ACR showing a rising trend.

Conclusion: This is a unique study where four novel UBM's were estimated, which appears to detect early DN without any significant difference between early and late diabetic nephropathy. Our ongoing longitudinal study shall clarify the range of different UBM in progressing phases of DN.

Notes: