Objective: Urine nerve growth factor (NGF), produced by the urothelium and bladder muscles, has been considered as a novel biomarker for diagnosis of overactive bladder (OAB) [1]. Bladder and urine NGF are higher than normal in patients with OAB, detrusor overactivity (DO), interstitial cystitis and bladder outlet obstruction with DO.

Diabetic uropathy, including diabetic cystopathy, erectile dysfunction and urinary tract infection, is found more than 80% of individuals with diabetes [2]. It has been suggested that OAB and storage problems are the main manifestations of bladder dysfunction in early stage of diabetes. Recently, we have found that men with type 2 diabetes and aged < 45 years have more lower urinary tract symptoms (LUTS) than controls and erectile dysfunction is associated with the severity of LUTS [3]. Thus, we hypothesize that urine NGF is elevated in the early stage of diabetes and urine NGF may be correlated with the severity of LUTS and erectile dysfunction. The aim of the study was to measure urine NGF levels in type 2 diabetic men < 45 years and to determine whether urine NGF levels could be a useful biomarker to assess the severity of LUTS and erectile dysfunction in the early stage of diabetes.

Methods: This study was approved by the institutional review board and ethics committee of this hospital. Informed consent was obtained from all subjects before study. In all, 62 men aged less than 45 years and with type 2 diabetes, who had regular follow-up for more than 6 months at our diabetic outpatient clinic, were consecutively enrolled. The medical history and concomitant diabetic complications of all patients were comprehensively reviewed. Urinary NGF levels were measured by enzyme-linked immunosorbent assay. The total urinary NGF levels were normalized to the concentration of the urinary creatinine (NGF/Cr) levels.

Participants were evaluate using the International Prostate Symptom Score (IPSS), Overactive Bladder Symptom Score (OABSS), the five-item version of the International Index of Erectile Function questionnaire (IIEF-5) and measurement of urinary flow rate and post-void residual urine volume. We invited 18 healthy staffs aged less than 45 years old in our hospital with a normal fasting blood glucose during the proceeding 1 year to be the control subjects. All data were expressed as mean standard deviation. Mean values of continuous variables were compared using Mann-Whitney U test. The Spearman correlation were used to examine urinary NGF/Cr levels associated with IPSS, OABSS, IIEF-5 and the parameters of uroflowmetry.

Results: The mean (SD, range) age of the diabetic patients was 40.0 (6.3, 19-45) years and the mean duration of diabetes was 4.0 (4.1, 0.5-20) years. Figure 1 showed that diabetic patients had significantly higher urinary NGF/Cr levels compared to the controls (0.52±1.2 versus 0.01±0.2, p=0.04). The urinary NGF/Cr levels were negatively correlated with IIEF-5 score (p=0.02, coefficient= -0.33, 0.06-0.55) and positively correlated with systolic pressure (p<0.001), diastolic pressure (p=0.01), neuropathy (p=0.02), retinopathy (p=0.03) and diabetic duration (p=0.04). The urinary NGF/Cr levels were not correlated with age (p=0.09), IPSS score (p=0.25), OABSS score (p=0.11), voided volume (p=0.60), peak flowrate (p=0.44), or postvoid residuals (p=0.19). Thirty-six patients with urinary NGF/Cr level <0.05 had higher IIEF-5 score than 26 patients with urinary NGF/Cr level ≥0.05 (20.5±5.0 versus 16.8±6.6, p=0.02) (fig.2).

Conclusion: Urinary NGF levels were elevated in type 2 diabetic men aged less than 45 years. Urinary NGF levels were correlated with erectile dysfunction but not correlated with LUTS, OAB symptoms or the parameters of uroflowmetry in these patients.

Reference: