IS THERE ANY IMPORTANCE TO DETERMINE UROMODULIN SERUM CONCENTRATION IN PATIENTS WITH LONG TERM DIABETES MELLITUS TYPE 2

E. Jordanova¹, S. Simic Ogrizovic^{2,3}, V. Samardzic⁴, V. Dopsaj⁵, Lj. Bokan⁶, G. Perunicic-Pekovic¹, J. Tica Jeftic⁴

¹Departmant of Nephrology, Clinic for Internal Medicine, Clinical Hospital Centre Zemun, Belgrade, School of Medicine, Belgrade, School of Medicine, Belgrade, Serbia; ⁴Departmant of Endocrinology, Clinic for Internal Medicine, Clinical Hospital Centre Zemun, Belgrade, Serbia; ⁵University of Belgrade, School of Pharmacy, Belgrade, Serbia; ⁶Departmant of Laboratory Diagnostics, Clinical Hospital Centre Zemun, Belgrade, Serbia

INTRODUCTION:

- Uromodulin or Tamm-Horsfall protein is 95kDa glycoprotein produced in the kidney by thick ascending limb of the loop of Henle.
- Although the physiological role of uromodulin is not clearly defined, there is a growing interest in determining this glycoprotein in serum and urine of patients with acute and chronic renal failure as a marker of renal function.
- The aim of the study was to evaluate uromodulin serum concentration in patients with long term typ 2 diabetes mellitus (T2DM).

METHODS:

- The study included 50 patients with T2DM mean age 50.8±15.1 years and 20 healthy controls. We determined the demographic characteristics of the patients, BMI; biochemical analyses: serum concentration of haemoglobin, urea, creatinine, microalbuminuria.
- Serum uromodulin was measured by ELISA method- test Euroimmun.
- The cystatin C level was determined by immunonephelometric method commercially test N Latex Cystatin C using nephelometer BN II System Assays (Siemens Healthcare).
- The glomerular filtration rate (eGFR) was calculated according to formulas:
- a) Cockcroft Gault GFR = [((140-age) x body weight)) / (72xserum creatinine)] x 0.85 (correction factor for female)
- b) MDRD (Modification of Diet in Renal Disease) GFR (mL/min/1.73 m²) = 175 × (serum creatinin)^{-1.154} × (age)^{-0.203} × (0.742 correction factor for female)



c) Simple Cystatin C GFR = 100 / serum Cystatin C

d) CKD - EPI (Chronic Kidney Disease Epidemiology Collaboration equation) GFR = 141 x min(S_{Cr}/κ , 1)^{α} x max(S_{Cr}/κ , 1)^{-1.209} x 0.993^{age} x 1.018 [female] x 1.159 [black]

RESULTS:

- The cross section study included 50 patients with T2DM: 18 males and 32 females and 20 healthy controls: 9 males and 11 females.
- Duration of T2DM was 10.4 ± 5.7 years (from 5 30 years).
- Glomerular filtration rate eGFR was 114.38±22.1ml/ min and microalbuminuria was 65.01±34.02 mg/l.

Table 1						
	BMI	Haemoglobin	Creatinine	CystatinC	Uromodulin	
	(kg/ m²)	(g/L)	(µmol/L)	(mg/L)	(ng/ ml)	
T2DM	31.27±5.59	133,86±13,08	$71,60 \pm 13.59$	$0,96 \pm 0,22$	$136,51 \pm 84,34$	
Control group	24.44±4.13	$146,45\pm15,42$	71,25±13,89	$0,78 \pm 0,08$	$220,50 \pm 92,39$	
Significance	p<0.01	p<0.01	p>0.01	p<0.01	p<0.01	

Table 2						
	Cockcroft Gault (ml/min)	MDRD (ml/min/1.73m ²)	Simple Cystatin C (mg/L)	CKD- EPI (ml/min)		
T2DM	$109,13 \pm 36,99$	88,91± 19,75	$108,73 \pm 21,26$	85,77± 15,78		
Control group	$132,96 \pm 39,5$	$105,44 \pm 20,47$	128,71±13,34	108,60±16,12		
Significance	p<0.01	p<0.01	p<0.01	p<0.01		

• Table 3 shows that we found a significant positive correlation between uromodulin and MDRD, simple Cystatin C and CKD EPI; but significant negative correlation between uromodulin and age, BMI and Cystatin C.

Table 3						
Variable	Coeffitient Correlation (r)	Significance (p)				
Age	-0.424	0.000				
BMI	-0.363	0.002				
MDRD	0.297	0.006				
Cystatin C	-0.226	0.010				
Simple Cystatin C	0.250	0.020				
CKD- EPI	0.367	0.002				





CONCLUSION:

- In the past few decades, serum creatinine has become the most commonly used marker of glomerular filtration rate and it is calculated with the following formulas: MDRD, Cockcroft Gault, CKD- EPI.
- Our results indicate that a higher serum uromodulin concentration is associated with better kidney function. Uromodulin increases with an increase in kidney function and behaves in a manner opposite to the conventional kidney function markers, which increases because of the retention due to decreased kidney function.
- Even though the role of serum uromodulin concentration is not established yet, it could be speculated that reduced serum concentration indicated early kidney damage in patients with long term T2DM.
- The study should be repeated on a larger group of patients.

LITERATURE:

1.Premaratne E et al. The impact of hyperfiltration on the diabetic kidney. Diabetes and Metabolism 2015; 41 (1): 5-17.

- 2. Scolari F, Izzi C, Ghiggeri GM. Uromodulin: from monogenic to multifactorial diseases. Nephrology DialysisTransplantation 2015; 30: 1250-1256.
- 3. Prajcer S et al. Evidence for a role of uromodulin in chronic kidney disease progression. Nephrology Dialysis Transplantation 2010; 25: 1896-1903.
- 4. Vyletal P, Bleyer A, Kmoch S. Uromodulin biology and pathophysiology an update. Kidney Blood Pressure Research 2010; 33: 456-475.
- 5. Bevc S et al. Simple cystatin C formula for estimation of glomerular filtration rate in overweight patients with diabetes mellitus type 2 and chronic kidney disease. Experimental Diabetes research 2012 (2012): 179849.

