

URINARY CYSTATIN-C: A NEW AUTOMATED PARTICLE-ENHANCED IMMUNE TURBIDIMETRIC TEST FOR THE ROUTINE EVALUATION OF KIDNEY TUBULAR FUNCTION

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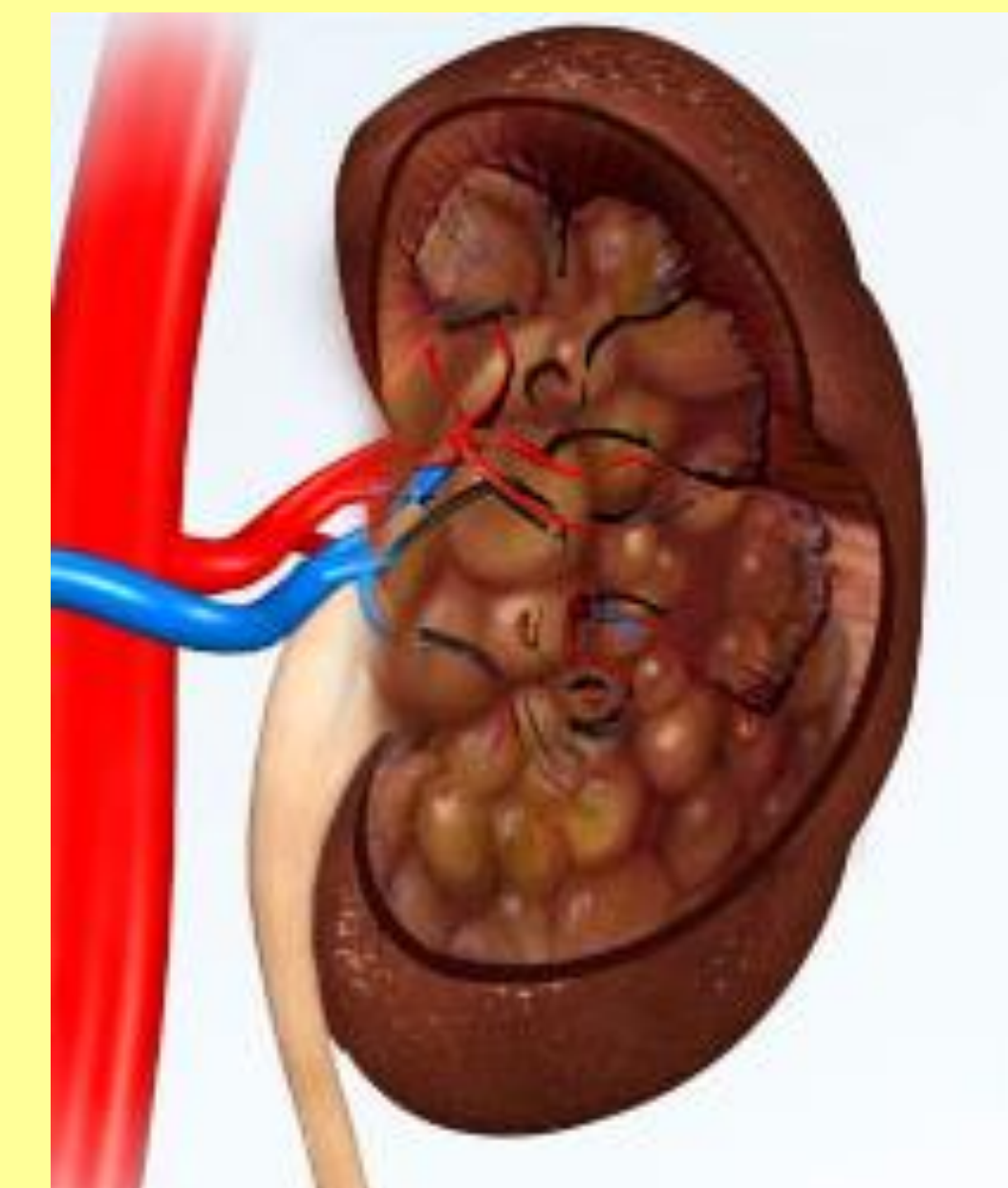
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BACKGROUND

Cystatin-C is an inhibitor of cysteine proteases with a molecular mass of 13 kDa. Due to its physical properties it is freely filtrated through the glomeruli then reabsorbed and almost completely catabolized by the proximal tubular cells. It is a normal component of urinary proteins in very low concentration. Recent studies showed that elevated levels of urinary cystatin-C (u-CYSC) reliably indicates tubular dysfunction.

AIMS

Because commercial u-CYSC test is not available at present, we optimized and validated an automated serum immune turbidimetric test for urine measurements. Furthermore, our aim was to investigate u-CYSC concentrations in diseases which can be accompanied by acute or chronic kidney injury.



METHODS

A particle-enhanced immune turbidimetric assay for serum CYSC (DiaSys GmbH) was adapted for a Cobas 8000/c502 automated analyzer (Roche) to measure u-CYSC.

PATIENTS AND SAMPLING

Control group

- Healthy individuals
- 40 male, 44 female
- Mean age: 39±12 years

Septic patients

- Sepsis-related acute kidney injury
- 18 male, 17 female
- Mean age: 68±13 years

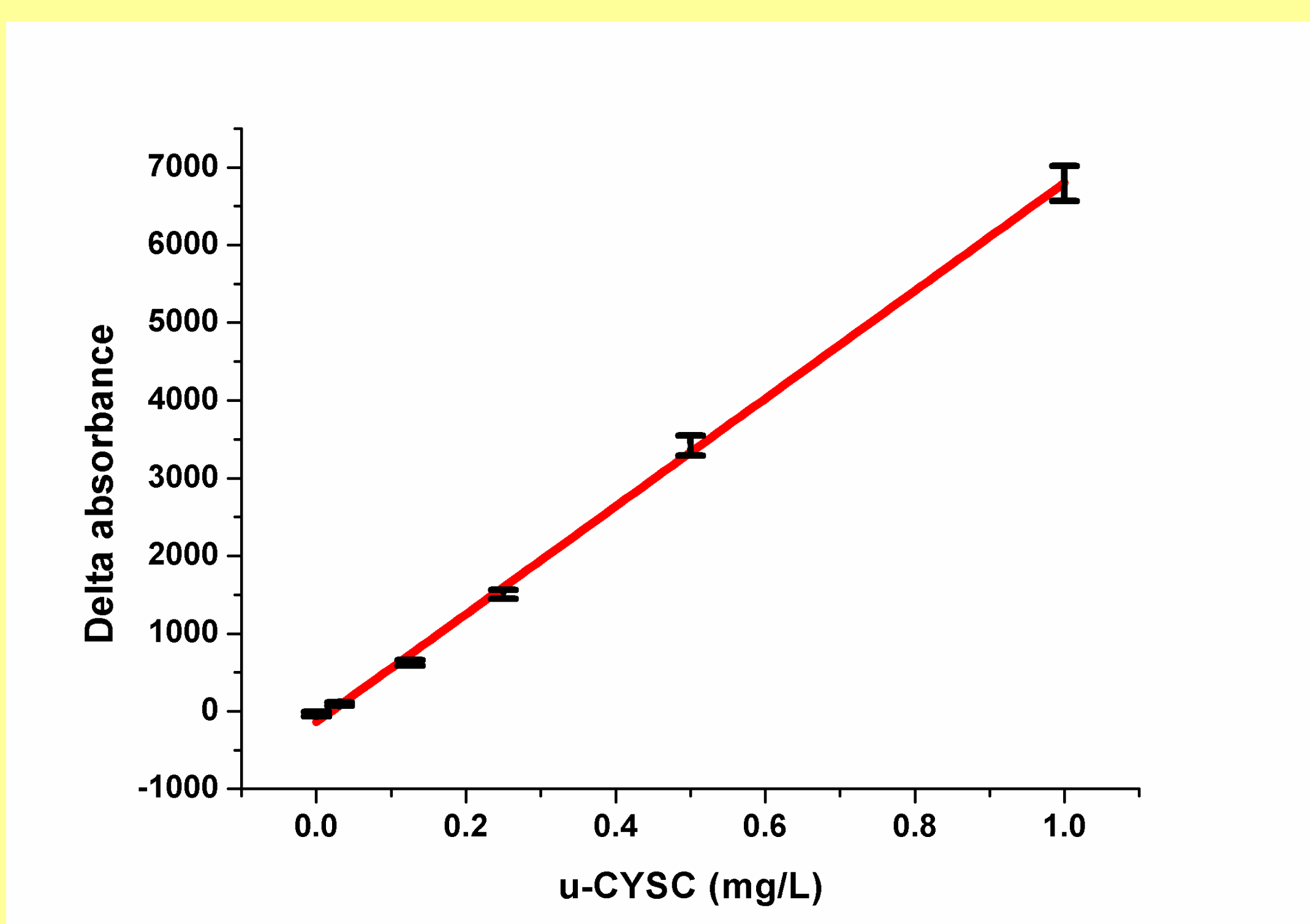
Patients with chronic hypertension

- 23 male, 20 female
- Mean age: 61±12 years

Spontaneous urine samples were analyzed.

Data were expressed in u-CYSC/creatinine ratios (mg/mmol).

RESULTS

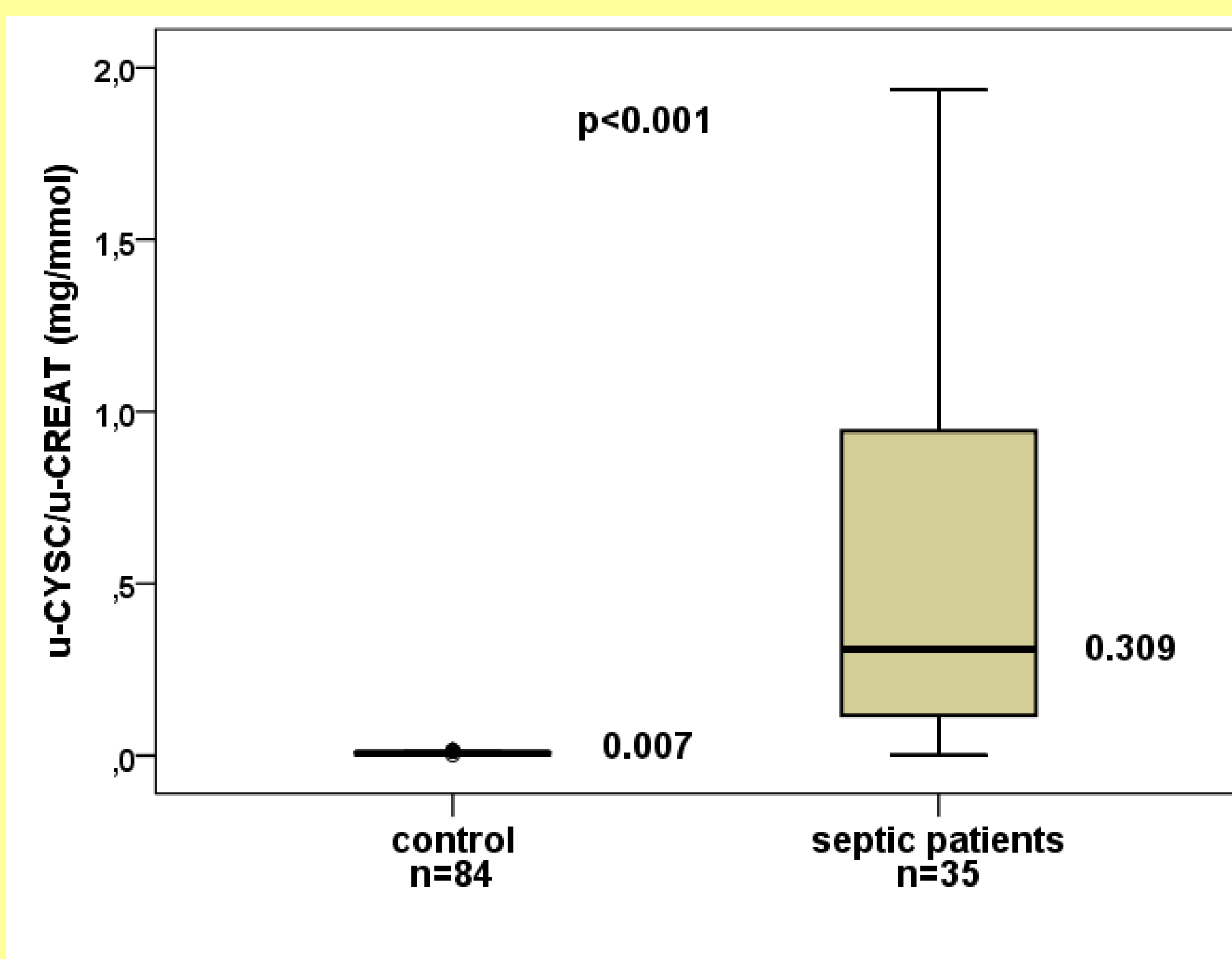


Calibration curve (0-1.0 mg/L) with linear graph fitting (n=30 separate calibrations, ±SDs are indicated)

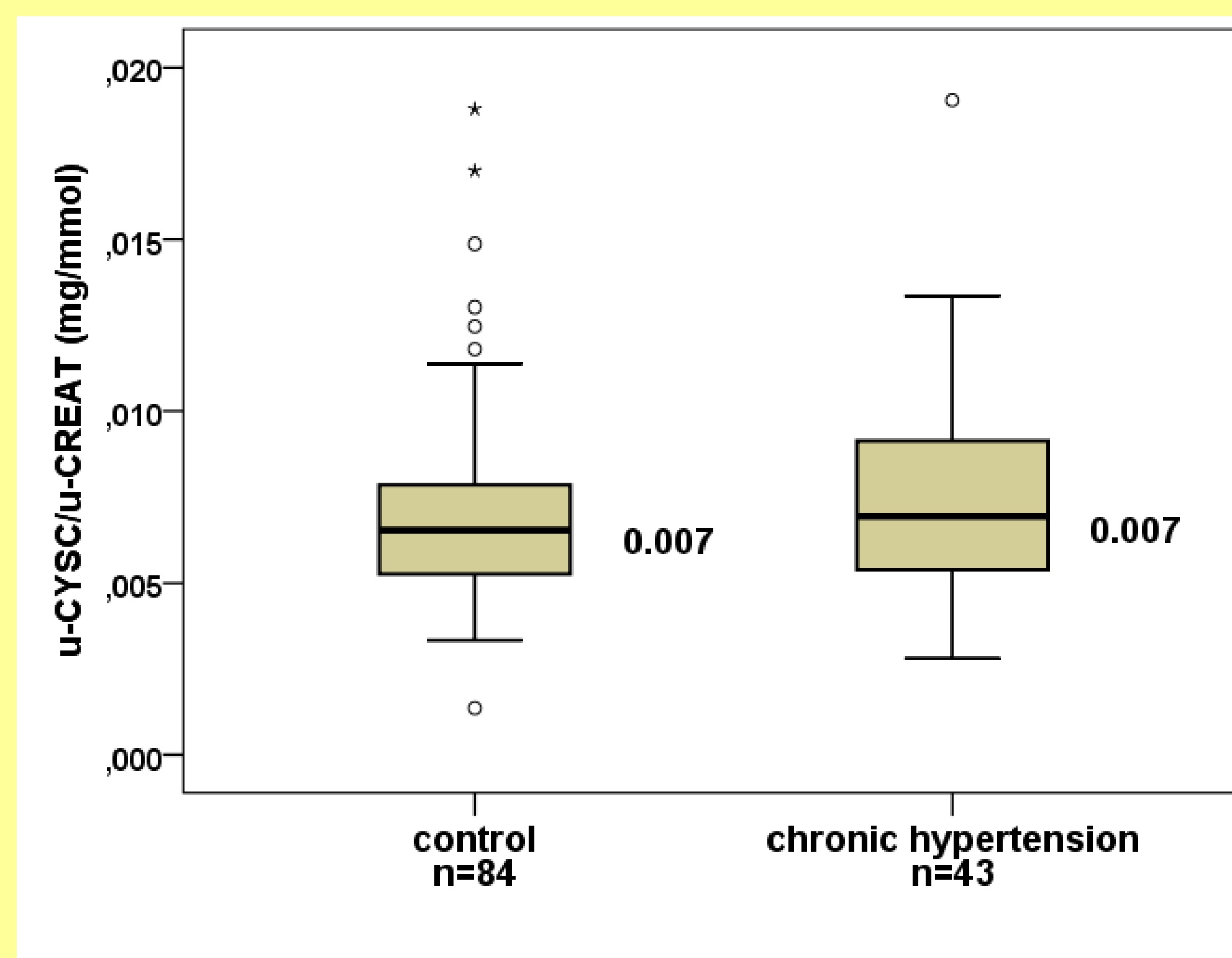
target value	intra-assay		inter-assay	
	CV %	accuracy %	CV %	accuracy %
0.728 mg/l	1.52	104.2	1.94	102.2
0.348 mg/l	1.79	99.4	1.90	96.9
0.073 mg/l	3.29	96.3	4.84	94.6

Imprecision and inaccuracy data of the u-CYSC assay at low, mid and high concentration levels

The **detection limit** was determined to be 0.017 mg/L u-CYSC. **Reference range** for u-CYSC/creatinine ratio was established to be 0.007 (0.004-0.015) mg/mmol [median (2.5-97.5 percentiles)]. Compared to the control group, u-CYSC/creatinine ratios showed approximately **44-fold elevation in sepsis-related acute kidney injury** (p<0.001). The u-CYSC/creatinine values of the chronic hypertension patient group did not differ significantly from those of controls.



Comparison of u-CYSC/u-CREAT ratios between controls and septic patients' group



Comparison of u-CYSC/u-CREAT ratios between controls and chronic hypertension patients' group

CONCLUSIONS

We adapted a highly sensitive, precise and accurate turbidimetric assay for CYSC determination in urine. Our **fully automated method** is ideal for routine lab testing and our findings confirm that u-CYSC levels **sensitively reflect the tubular damage in acute kidney injury**.