SERUM αKLOTHO IS ASSOCIATED WITH PATHOLOGICAL CHANGES IN RENAL TISSUE IN PATIENTS WITH STAGES 1-3 CKD

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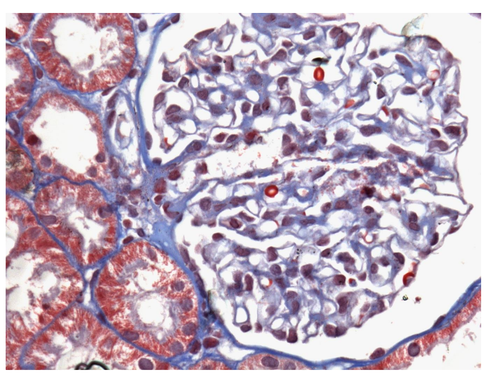
INTRODUCTION AND AIMS

It is well known that chronic kidney disease (CKD) is associated with Klotho deficiency. It is suggested that renal and serum Klotho levels start to decline in stage 2 of CKD and urinary Klotho can be probably earlier - in stage 1. It is believed that soluble Klotho could serve as an early and sensitive biological marker of kidney function decline. According to experimental data Klotho deficiency is not just a biomarker, but a pathogenic factor for CKD progression. The aim of our study was to analyze the levels of Klotho in renal tissue, serum, and urine of patients with CKD 1-3 stages and investigate the association pathological changes of renal tissue and Klotho levels.

METHODS

In cross-sectional study 80 patients [36 male, 44 female; age 34 (27; 54) years] undergoing kidney biopsy with primary glomerulopathies and stages 1 (N=26), 2 (N=25), 3 (N=29) of CKD were included. According the results of light microscopy 38 (48%) patients had IgA-nephropathy, 16 (20%) – focal segmental glomerulosclerosis, 14 (17%) – membranous nephropathy, 12 (15%) – minimal change disease. Samples of serum and urine were obtained on the day of biopsy. Serum and urinary Klotho (ELISA), renal expression of Klotho (IHC, morphometric analysis) were analyzed. Pathological changes of renal tissue were evaluated as indices – the index of glomerulosclerosis (IGS, %) and the index of tubular and interstitial damage (TID, score):



IGS (%) = [[GGS + 0.5 SGS]/N] •100%

GGS – the number of glomeruli with global glomerular sclerosis (GS), SGS – the number of glomeruli with segmental GS, N – the number of glomeruli in renal biopsy

TID (score) = 1/3 [GD+VD+HD] + TA + IF

GD - granular, VD - vacuolar and HD - hyaline droplet tubular degeneration, TA - tubular atrophy, IF - interstitial fibrosis

RESULTS

We observed the total decline of Klotho in early CKD. The level of renal Klotho (rKlotho) was significantly lower in CKD in stage 2 and serum Klotho (sKlotho) – in stage 3 compared to stage 1 ($p<0.04$), while there were no differences in urinary Klotho (uKlotho) levels in stages 1-3 CKD ($p>0.099$). The level of sKlotho was highly associated with IGS (fig. 1 a) and TID (fig. 1 b). There were no significant correlations between the indices of renal tissue damage and rKlotho (IGS: r=-0.13, p=0.32; TID: r=- 0.21, p=0.13), uKlotho (IGS: r=- 0.05, p=0.72; TID: r=- 0.07, p=0.62).

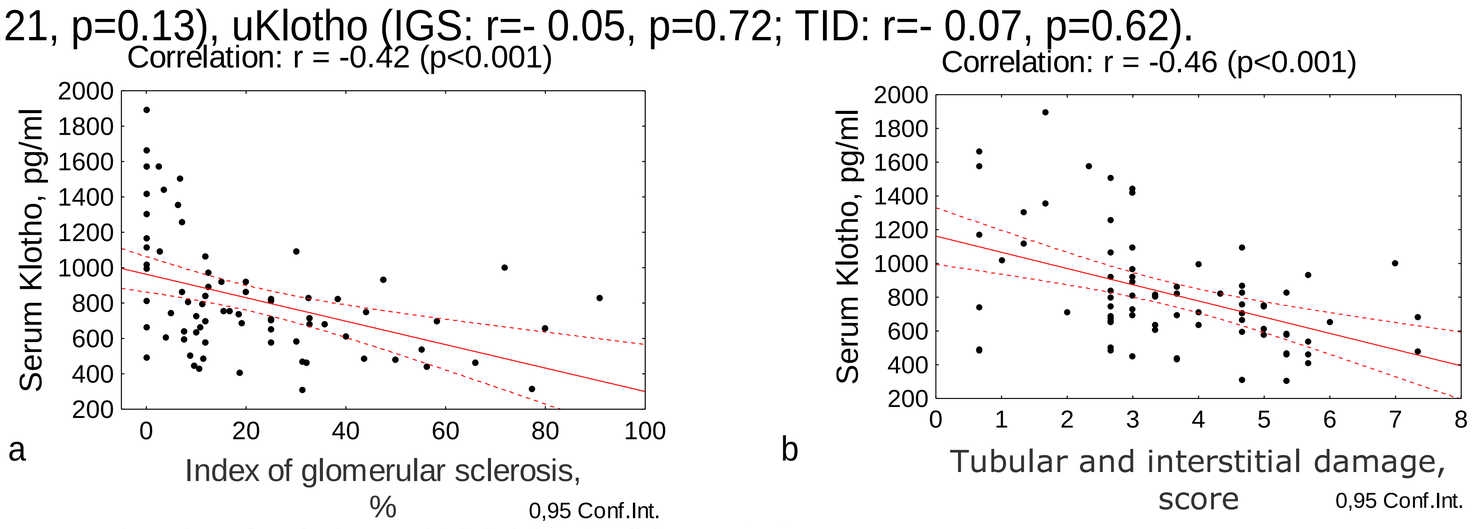


Figure 1. The plot of sKlotho and IGS (a), TID (b) correlation

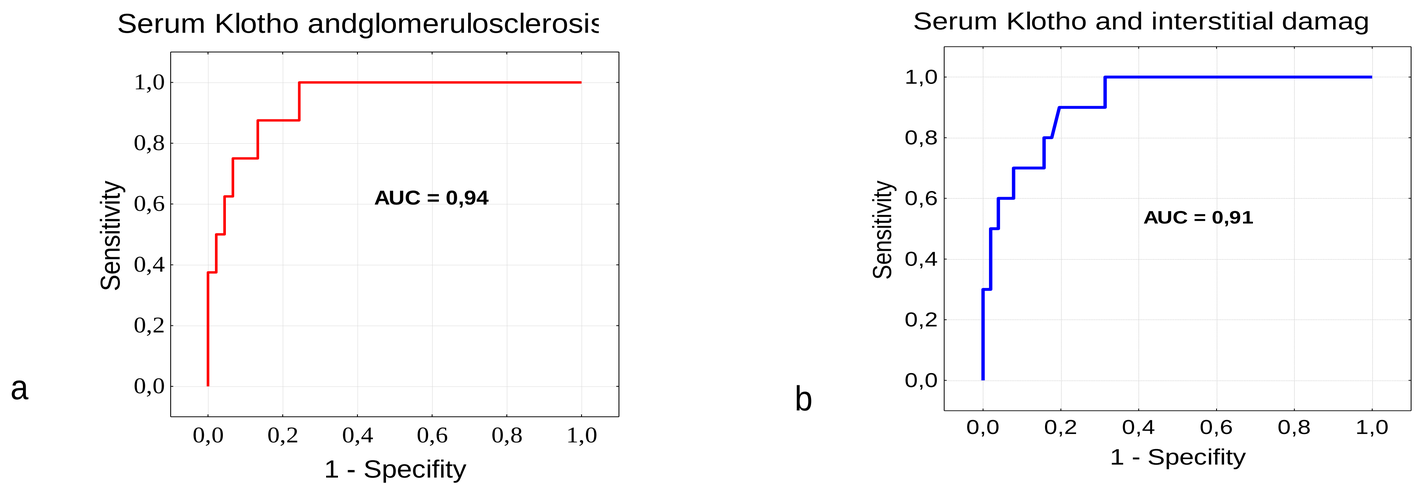


Figure 2. Receiver Operating Characteristic (ROC) Curve: serum Klotho and glomerular sclerosis (a) and tubular interstitial damage (b)

Diagnostic performance of serum Klotho in glomerulosclerosis, tubular and interstitial damage illustrated in figure 2. The AUC for the detection of glomerulosclerosis was 0.94 (fig. 2 a), for total tubular and interstitial damage – 0.91 (fig. 2 b).

CONCLUSION

The results of this study support that sKlotho is associated with common causes of CKD progression – sclerosis of glomeruli, tubular atrophy and interstitial fibrosis, the measurement of serum Klotho level allows detection of glomerulosclerosis and total interstitial damage in CKD patients.

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