INTRODUCTION AND AIMS: Epithelial-mesenchymal transition (EMT) enables migration of tubular epithelial cells and their transformation into myofibroblasts, leading to renal interstitial fibrosis and, finally, to chronic kidney disease (CKD). Transforming growth factor (TGF) beta1 is the master regulator of fibrosis and the main EMT player, whereas matrix metalloproteinases are known for their role in the regulation of extracellular matrix content and tissue remodeling and they have recently been suggested of inducing EMT. However, the knowledge on survivin and E-cadherin influence on those processes is limited and the latter has not been analyzed in the CKD population so far. The aim of study was to assess the concentrations of survivin, E-cadherin, MMP-2, MMP-9 and TGFbeta1 in serum and urine of children with advanced stages of CKD, to examine the correlations between them and with other markers of EMT-related apoptosis, such as death receptors sFas/sFasL and anti-apoptotic heat shock protein Hsp27.

METHODS: 41 children with CKD stages 3 to 5 (aged 4-17 years, mean eGFR 26ml/min/1.73sq.m.) and 23 age-matched healthy controls were enrolled in the study. The serum and urine concentrations of analyzed parameters were assessed by ELISA.

RESULTS: The median serum values of survivin, E-cadherin, MMP-2, MMP-9 and TGFbeta1 were significantly elevated in CKD patients vs. controls. The urine levels of examined parameters, normalized to urine creatinine, were also significantly increased when compared to the control group. All urine markers correlated with each other, with the strongest relations between MMP-9, TGFbeta1 and E-cadherin, and all, except for survivin and TGFbeta1, correlated significantly with the corresponding values in serum. Urine parameters were also related to apoptosis indices in serum. Serum E-cadherin was the only parameter correlating with eGFR. None of the analyzed parameters correlated with hsCRP or other biochemical markers.

CONCLUSIONS: The increased urine levels of survivin, E-cadherin, MMPs and TGFbeta1 may indicate tissue remodeling and EMT-related apoptosis, resulting in renal interstitial fibrosis characteristic for chronic kidney disease. Urine MMP-9, TGFbeta1 and E-cadherin form the panel of markers describing similar features of EMT-related processes, whereas urine survivin may be considered a new independent biomarker of kidney-specific EMT.