Neutrophil Gelatinase-Associated Lipokalin & Cathepsin as an Early Predictors of Kidney Dysfunction in Diabetic Children.

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**Introduction / Aims**

One of the most dangerous complications of diabetes mellitus (DM) is diabetic kidney disease (DKD). At present, the measurement of albuminuria and glomerular filtration is used as a standardized non-invasive test for the diagnosis of DKD. However, early renal dysfunction may be overlooked despite using that method.

The aim of this study was to evaluate the level of neutrophil-gelatinase associated lipocalin in serum (sNGAL) and in urine (uNGAL) as well as urinary excretion of cathepsin L (uCatLH) and angiotensinogen (uAGT) in children with type 1 DM (DM1) considered as not presenting DKD. We also assessed the relations between these biomarkers and albumin/creatinine ratio (ACR), estimated glomerular filtration rate (eGFR), glyemic control and duration of diabetes.

**Methods**

- The study group consisted of 63 children with DM1 (28 males and 35 females) with mean age of 13.46±2.95 yr.
- The average time of treatment was 5.16±3.39 yr. All patients presented a normal albumin/creatinine ratio (ACR < 30 mg/g) and normal eGFR, based on cystatin C (>90 ml/min/1.73m²).
- Glomerular hyperfiltration (GH) was defined as an eGFR value above 135 ml/min/1.73m².
- The control group consisted of 22 healthy, age and gender matched children.

**Results 1**

Children with DM1 compared to controls showed significantly higher levels of uNGAL (43.02±45.68 vs. 6.85±6.05 ng/ml; p<0.001), as well as lower sNGAL (109.96±50.06 vs. 151.34±53.95 ng/ml; p<0.001) and uCatL (4.32±1.61 vs. 5.16±0.95 ng/ml), table 1, figure 1. These changes were observed even in children treated for less than 5 years because of diabetes and with optimal glycemic control (HbA1c<7.5%), uAGT levels were similar in both groups (0.148±0.474 vs. 0.00 ng/ml; p=0.628).

**Results 2**

GH was recognized in 30% of children. These patients showed a significantly higher value of uNGAL, uCatL and ACR as well as lower value of sNGAL presented poor glycemic control with respect to non-GH patients.

A positive correlation between uNGAL and ACR (r=0.313; p=0.013) was found (figure 2), as well as between uCatL and eGFR (r=0.501; p=0.034). HbA1c levels showed a positive correlation with eGFR (r=0.399; p=0.014) and with ACR (r=0.268; p=0.034). In the subgroup with GH, a significant inverse correlation between uNGAL and sNGAL (r=−0.580; p=0.048) was found.

**Conclusions**

- Normal-range albuminuria and normal eGFR do not exclude DKD, if defined as changes of sNGAL, uNGAL and uCatL
- These changes may occur even in children with relatively short lasting diabetes and with optimal glycemic control.
- The mechanism of early kidney damage may be associated with tubular damage and GH.
- Our study highlights the value of sNGAL, uNGAL and uCatL as potential markers for early DKD detection.