CLINICAL SIGNIFICANCE OF URINARY MARKERS OF PODOCYTES DAMAGE IN PATIENTS WITH DIABETES MELLITUS (DM).

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INTRODUCTION AND AIMS

One of the earliest clinically detectable abnormalities in diabetic nephropathy (DN) is microalbuminuria (MAU) that eventually progresses to proteinuria (PU). The degree of PU correlates with the progression of glomerulosclerosis and tubulointerstitial fibrosis. More recently, biopsy studies in humans with DN have provided strong evidences that podocytes are injured very early and are involved in glomerular permeability acceleration and glomerulosclerosis initiation.

The aim of the study was to assess urinary biomarkers of Pdc damage in DM pts with different AU/PU and renal dysfunction, to clarify their significance for early DN diagnostics and progression risk assessment.

METHODS

74 DM pts were studied (type 1 DM (T1DM) - 30, type 2 DM (T2DM) - 44), including 41 pts with normoalbuminuria (NAU) (I group), 13 pts with c MAU (II group), 20 pts with PU (III group). GFR>90 ml/min was revealed in 41pts, GFR 90-60 ml/min – in 25 pts, GFR<60 ml/min – in 8 pts. Arterial hypertension (AH) was observed in 52 pts (70%), mainly in T2DM. 8 healthy subjects were studied as control. Urinary levels of nephrin (an important slit diaphragm protein with anti-apoptotic signaling properties) and podocin were measured by ELISA.

RESULTS

High nephrinuria (NU), which not detecting in controls (> 5,84 ng/ml), was revealed in 63% of pts with NAU, in 77% - with MAU, in 80% - with PU (fig.1) The mean NU levels in pts with NAU and MAU did not differ in T1DM and T2DM, that reflect common mechanisms of podocytes damage. The mean level of NU in pts with PU was significantly higher than in DM with MAU and NAU (p<0,05). Similar regularities were noted for podocinuria (PdU). High PdU (>1,73ng/ml) was revealed in 78% of DM pts with NAU and its frequency increased in overt nephropathy (83%) (fig.2). Direct correlation was obtained between NU and AU (R=0,47 p=0,03), this relationship was more strong in pts with MAU (R=0,947 p=0,01).

NU and PdU in T1DM correlated directly with serum creatinine level (R=0,489 p=0.009 for NU and R=0,468 p=0,02 for PdU) and indirectly with GFR (R=-0,461 p=0,02), emphasizing the role of podocytes damage not only in glomerular permeability, but also in glomerulosclerosis formation. In pts with GFR<60 ml/min, regardless of DM type, there was direct relationship between the NU level and DM duration (fig.3). In DM duration less than 5 years NU correlated directly with HвA1c level (fig4). These data reflect the key role of a hyperglycemia in podocytes dysfunction and emphasize the importance of glycemic control from the DM onset. AH had an influence on the NU level, reflecting the hemodynamic mechanism of podocytes injury. We revealed direct correlation between systolic BP and NU, it was significant in T2DM (R=0,33 p=0,029). We believe that it is connected with the greater AH frequency in T2DM. These pts were more senior, many of them already had AH before DN development.

Fig. 1. Nephrinuria (NU) in DM patients

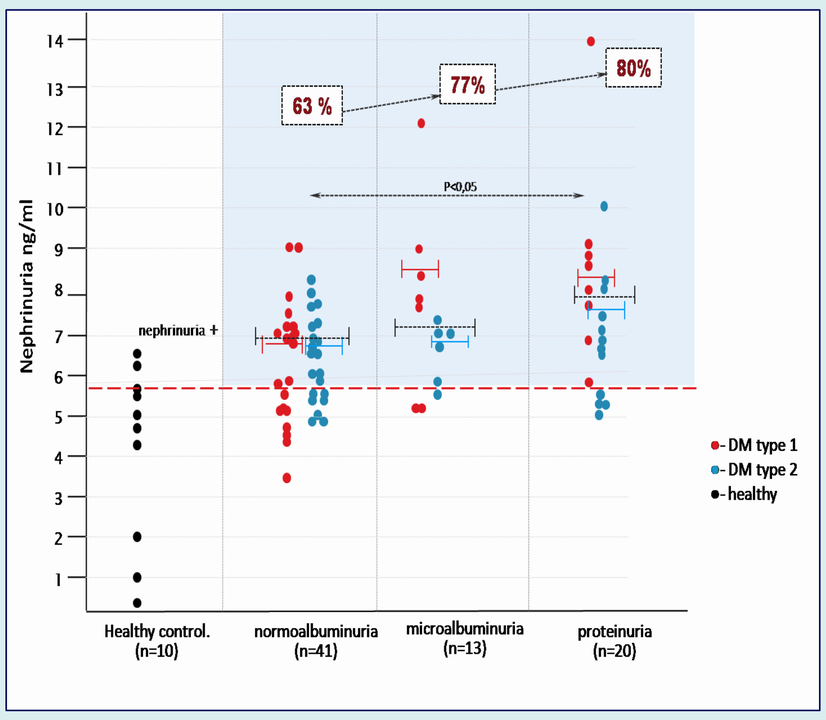


Fig. 2. Podocinuria (PdU) in DM patients

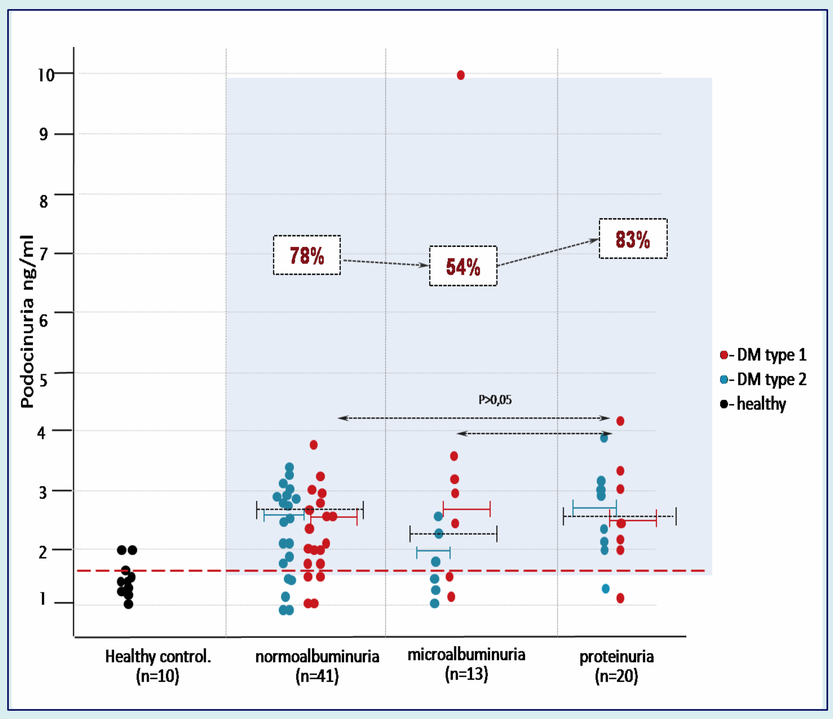


Fig.3. Correlation between NU and DM duration

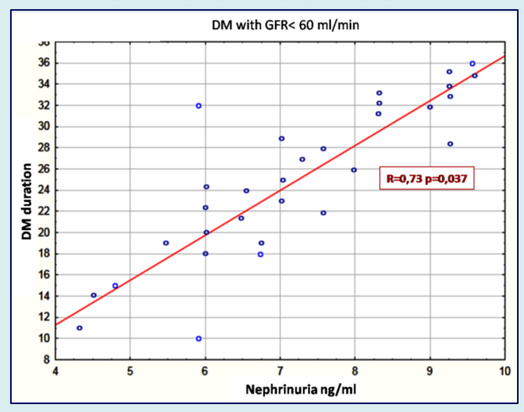
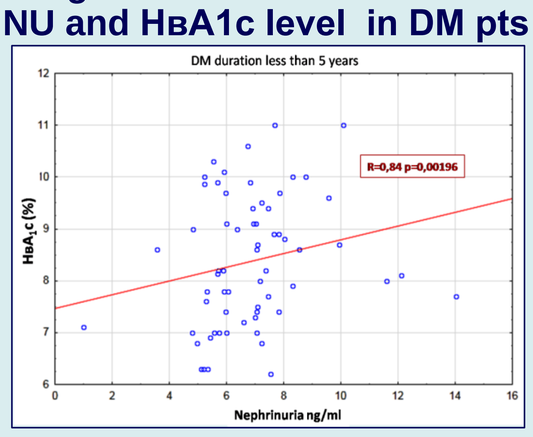


Fig. 4. Correlation between NU and HвA1c level in DM pts



CONCLUSION

High urinary levels of podocytes damage markers reveal in many DM pts, preceding the development of clinically significant AU. The level of these indicators depends on DM duration, severity of glycemia and AH. Determination of NU and PdU levels can be useful tests for early identification and monitoring of glomerular damage in DM.

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