EVALUATION OF ABILITY OF URINARY PODOCALYXIN, NEPHRIN AND LIVER TYPE FATTY ACID BINDING PROTEIN FOR EARLY DIAGNOSIS IN RENAL INJURY IN ADOLESCENTS WITH TYPE 1 DIABETES

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BACKGROUND

Early identification of diabetic nephropathy (DN) is crucial because it creates opportunity for preventing the incidence of DN and/or even slows down the process of end-stage renal disease attributed to diabetes.

Currently, microalbuminuria is generally thought to be an early marker of DN in clinical practice. However, recently emerging evidences suggested that glomerular damage also presented in diabetes patients with normoalbuminuria, who might easily missed diagnosis if only detecting microalbuminuria.

We aimed to determine the place of biomarkers that related different segments of the glomeruli, called podocalyxin (PCX), nephrin and liver type fatty acid binding protein (L-FABP), detecting diabetic kidney injury in normoalbuminuric and normotensive adolescents with type 1 diabetes.

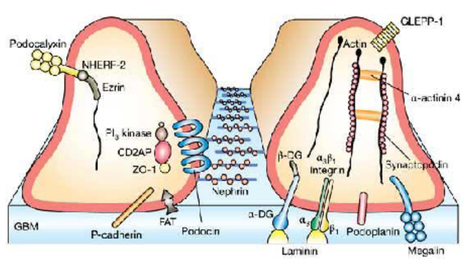


Figure 1. Podocalyxin is the major surface antigen of podocytes. The number of podocytes reduced in diabetic kidney. Podocytes detachment presented in diabetes patients with normoalbuminuria might be a possible marker of early stage of nephropathy.

Nephrin is podocyte slit-diaphragm associated protein. Recently, studies have described presence of nephrin in the urines of Type I diabetic patients even in the absence of microalbuminuria or normoalbuminuria.

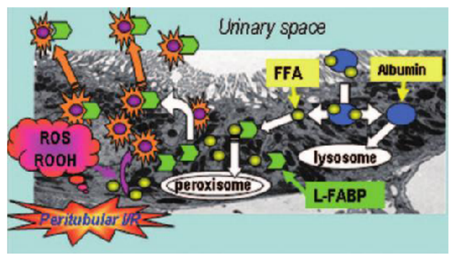


Figure 2. Renal L-FABP mechanism. In oxidative process, lipid peroxidation products will accumulate in, and damage proximal tubules. L-FABP is presumably capable of binding lipid peroxidative products and transferring them to urinary spaces. LFABP is excreted from the proximal tubules into urine by binding cytotoxic lipids.

STUDY DESIGN

One hundred thirty adolescents with type 1 diabetes were enrolled in the study.

The inclusion criteria for the study were: absence of urinary tract diseases or infection, and no history of hypertension, fever, acute illness, and other renal diseases except DN. The patients had nephrotoxic drug within 4 weeks also were excluded.

All subjects had intensive insuline therapy.

Thirty healthy volunteers were randomly selected as controls. The inclusion criteria were: no history of hypertension, diabetes, renal disease or vascular disease, matched for age.

Three different study groups were created according to different variabls (Figure 3).

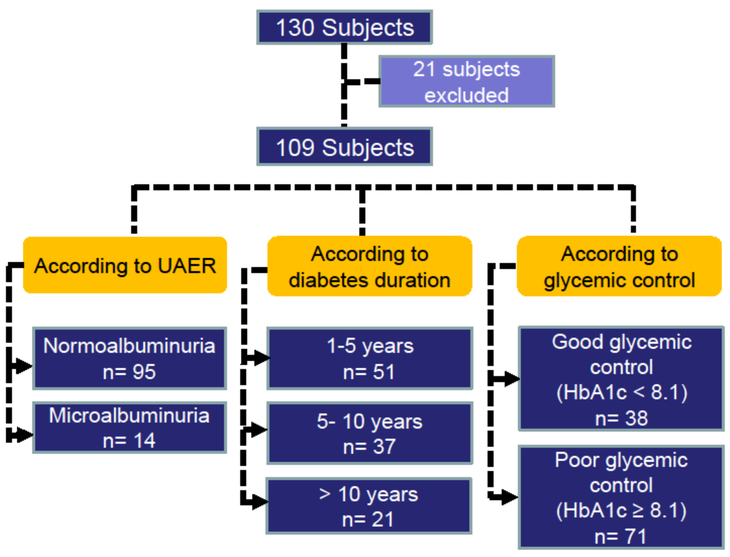


Figure 3. Study groups

Clinical data including the age, gender, body mass index (BMI), blood pressure were collected for all subjects. First-morning urines and peripheral venous blood samples were obtained from subjects. Urine and serum samples were detected within 30 minutes after collection. Albumin and creatinine were analysed in both spot urine and 24- h collected urine by immunoturbidimetry. PCX, nephrin, L-FABP measurements were performed in spot urine by Elisa method.

Glomerulary filtration rate (GFR), was calculated with the formula below.

$$GFR = \frac{\text{Urinary creatinine (mg/dL)x urinary volume (mL/d) x 1.73 (mL/dk/1.73 m}^2\text{)}}{\text{Serum creatinine (mg/dL) x 1440 x Body surface area (m}^2\text{)}}$$

RESULTS

The adolescents with tip 1 diabetes and healthy subjects have similar auxological and descriptive data. GFR was in normal range in all subjects, and controls.

Urinary podocalyxin, nephrin, L-FABP levels were increased before the development of hyperfiltration, and were higher in diabetic subjects compared with nondiabetic healthy subjects (Figure 4).

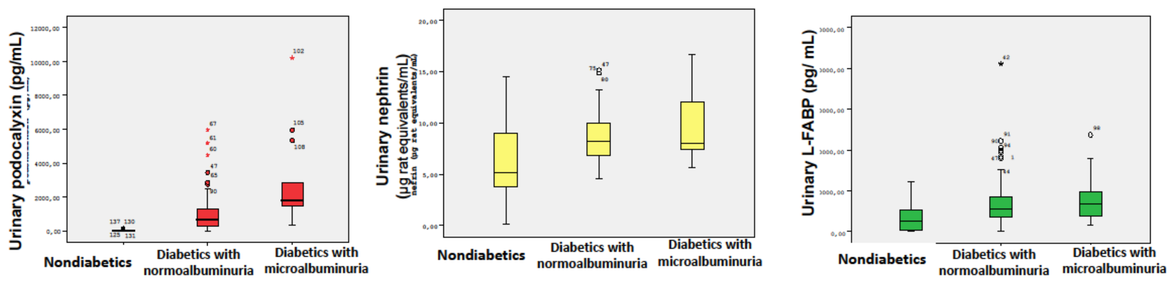


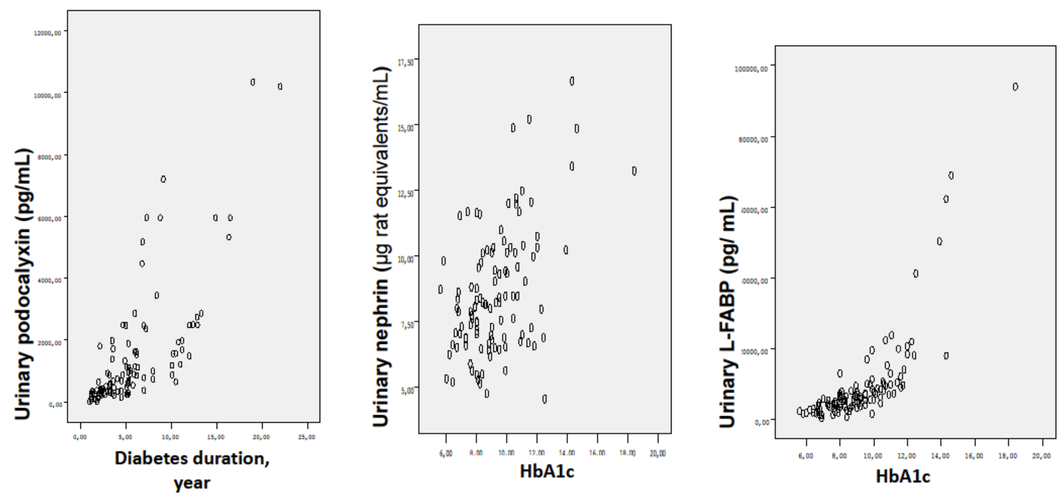
Figure 4. Urinary podocalyxin, nephrin and L-FABP levels.

Excretion of albumin in spot urine was similar among the groups created according to duration of diabetes.

Albumin excretion in the urine collected for 24 hours was increased with duration of diabetes.

Similarly PCX in spot urine was associated with diabetes duration (r=0.752, p>0.001). The subjects had diabetes more than ten years had the highest level of PCX.

PCX was associated with mean HbA1c (r=0.24, p=0.01) (Figure 5).



Urinary nephrin and L-FABP levels were associated with glycemic control. (r=0.45, p=<0.001 ve r=0.69, p=<0.001). The diabetic subjects with poor controlled diabetes have increased levels of nephrin and L-FABP (Figure 5). Excretion of albumin in both spot urine and 24-h-collected urine was increased in the diabetics with poor control. On the other hand GFR was similar in both good controlled and poor controlled groups.

In subjects with microalbuminuria, urinary PCX, nephrin, L-FABP levels were extremely elevated compared with normoalbuminuric subjects. Nevertheless, increase of these urinary biomarkers were detected in normoalbuminuric subjects.

CONCLUSION

The present study demonstrates that elevated urinary podocalyxin, nephrin and L-FABP excretion may determine early kidney injury before microalbuminuria occurs. Besides, these biochemical markers may be useful for staging kidney injury, predicting kidney injury progression and monitoring response to therapy. Closer monitoring of diabetic patients with elevated urinary podocalyxin, nephrin, L-FABP levels and protective measures may prevent chronic kidney disease development.

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