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NLRP3 inflammasome expression and urinary *HSP72* in relation to biomarkers of inflammation and oxidative stress in diabetic nephropathy patients

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Diabetic nephropathy (DN) is one of the major causes of end-stage renal disease. Nod-like receptors nucleotide-binding domain and leucine-rich repeat pyrin-3 domain (NLRP3) inflammasome displays a considerable role in the chronic inflammatory state observed in diabetic patients. Urinary heat shock protein 72 *(uHSP72)* is a sensitive and specific biomarker for the early detection the acute kidney injury. The aim of this study was to evaluate NLRP3 relative gene expression, its correlation with inflammatory and oxidative stress markers, and to assess the value of u*HSP72* in the early detection of DN in type 2 diabetic patients with different degrees of DN. Forty-five type 2 diabetic patients were enrolled in this study: 15 normoalbuminuric; 15 microalbuminuric; 15 macroalbuminuric patients in addition to 15 healthy controls. Clinical examination and routine laboratory investigations were done. NLRP3 mRNA expression was assessed by real time PCR. Serum 8-hydroxy-2'-deoxyguanosine (8-OHdG), IL-1β and u*HSP72* levels were estimated by enzyme-linked immunosorbent assay. Serum chitotriosidase (CHIT1) activity was examined. Significant higher NLRP3 mRNA expression, serum 8-OHdG, IL-1β and u*HSP72* levels, in addition to CHIT 1 activity were documented in the macroalbuminuric patient group as compared to the other two diabetic and control group. They were significantly positively correlated and to urinary albumin/creatinine ratio, serum creatinine and HA1c. Multiple linear regression analysis using UACR as dependent variable, confirmed that u*HSP72*, and relative NLRP3 mRNA expression were the independent predictors of DN (β were 0.432 and 0.448 respectively, P<0.001). Receiver operating characteristic analyses revealed that both NLRP3 mRNA expression and u*HSP72* levels were useful biomarkers discriminating DN patients from T2DM patients (AUC were 0.957 and 0.983 respectively) In conclusion, u*HSP72* may be considered as a novel potential diagnostic biomarker for the early detection of DN. Moreover, these data support the pivotal role of NLRP3 in the development and progression of DN.

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