

## **Up-regulation of HIF-1 $\alpha$ in patients with diabetic nephropathy.**

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### **Abstract**

**Objective:** To study role of HIF-1 $\alpha$  in patients with diabetic nephropathy.

**Methods:** This study selected a total of 133 participants including 61 patients with type 2 diabetes but no nephropathy, 49 patients with diabetic nephropathy and 23 healthy individuals as a control at Anhui provincial hospital during January 2012 to December 2016. Nephropathy was identified according to historical estimated glomerular filtration rate (eGFR). Parameters such as Fasting Blood Sugar (FBS), Blood Urea Nitrogen (BUN), Urine Albumin Creatinine Ratio (UACR) were also tested and recorded. Biopsy assessment was conducted when renal function or urinary abnormalities was inconsistent with the clinical expression or the natural history of DN. Western blotting was used to test the expression of serum HIF-1 $\alpha$  in all patients and the control.

**Results:** Values of FBS, BUN and UACR were all significantly higher in DN and diabetes groups compared with the healthy control. Meanwhile, values of FBS, BUN and UACR were also all significantly higher in DN patients compared with the diabetes patients with no nephropathy. eGFR in DN patients was significantly lower than other two groups. No obvious lesion was observed in the diabetes patients with no nephropathy. However in DN patients, pathological changes were obvious in tubulointerstitia. In DN patients, expression of HIF-1 $\alpha$  was significantly higher than both diabetes patients with no nephropathy and the healthy control,  $P < 0.05$ . Patients with large amount of albuminuria showed highest expression of HIF-1 $\alpha$  compared with other groups. However, HIF-1 $\alpha$  in normo-albuminuria and micro-albuminuria groups showed no significant difference.

**Conclusion:** HIF-1 $\alpha$  was up-regulated in patients with diabetic nephropathy. This study may give clinical basis to the role of HIF-1 $\alpha$  in development of diabetic nephropathy. However, further studies are still needed to make deeper insights to illuminate HIF-1 $\alpha$  in DN patients.

**Keywords:** HIF-1 $\alpha$ , Diabetic nephropathy, Clinical expression.

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### **Introduction**

Among various complications of diabetes, the Diabetic Nephropathy (DN), which is characterized as features of the increase of Urinary Albumin Excretion (UAE) rate, abnormal plasma creatinine level, abnormal Glomerular Filtration Rate (GFR) or calculated creatinine clearance [1], is one of the major causes of morbidity and mortality for diabetic patients and also the leading cause of End-Stage Renal Disease (ESRD) in Western countries affecting 20%~40% patients requiring dialysis and or transplantation [2]. In developing countries, the incidence of DN is also increasing rapidly [3]. Studies showed that diabetes with proteinuria is a high risk factor of ESRD for diabetic patients [4,5] and the incipient DN, which is recognized as remission/regression of microalbuminuria, is a common feature for both type 1 and 2 diabetes mellitus [6]. Researches for progression of DN demonstrate that DN is associated with lots of biology progresses such as oxidative stress [7], inflammation [8] and hypoxia [9]. However, deeper understanding for mechanisms of DN is still insignificant.

It has been proved that hypoxia is an acknowledged pathway to nephropathy, and is related to mechanism for the development of DN [9]. Hypoxia-Inducible Factor-1 (HIF-1) is the key mediator in process of cellular oxygen balance [10]. It allows the adaptive responses to hypoxia by participating in progress of cellular energy metabolism, glucose transport, angiogenesis, and so on. HIF-1 can also regulate particular genes involved in hypoxia, such as erythropoietin, vascular endothelial growth factor A and enzymes associated with glucose metabolism [11]. HIF-1 $\alpha$  is one of the two subunits of HIF-1 which has been proved to play a crucial role in process of cellular hypoxia. Regulation of HIF-1 activity is critically dependent on the degradation of the HIF-1 $\alpha$  [12].

Recently, several studies showed that HIF-1 $\alpha$  is up-regulated in DN animals [13,14]. However, to our best knowledge, HIF-1 $\alpha$  in DN patients has not been reported yet. In the present study, we investigated expression of HIF-1 $\alpha$  in DN patients and studied relationship of HIF-1 $\alpha$  and DN risk factors.