

CIRCULATING CXCL16 IN DIABETIC KIDNEY DISEASE

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Objectives:

Cardiovascular disease (CVD) is one of the top causes of death in CKD patients. Chronic low grade systemic inflammation and lipid abnormalities are thought to play a role. Inflammatory cytokines such as interferon gamma (IFN γ) and tumor necrosis factor alpha (TNF α) promote Chemokine (C-X-C) ligand 16 (CXCL16) expression. CXCL16 has been implicated in the pathogenesis of vascular, kidney and lung injury. CXCL16 is a small cytokine and cell surface receptor that has been linked to lipid metabolism and to vascular disease. A better understanding of the factors contributing to the high mortality may help design novel monitoring and therapeutic approaches.

To identify factors influencing plasma CXCL16 in diabetic kidney disease patients.

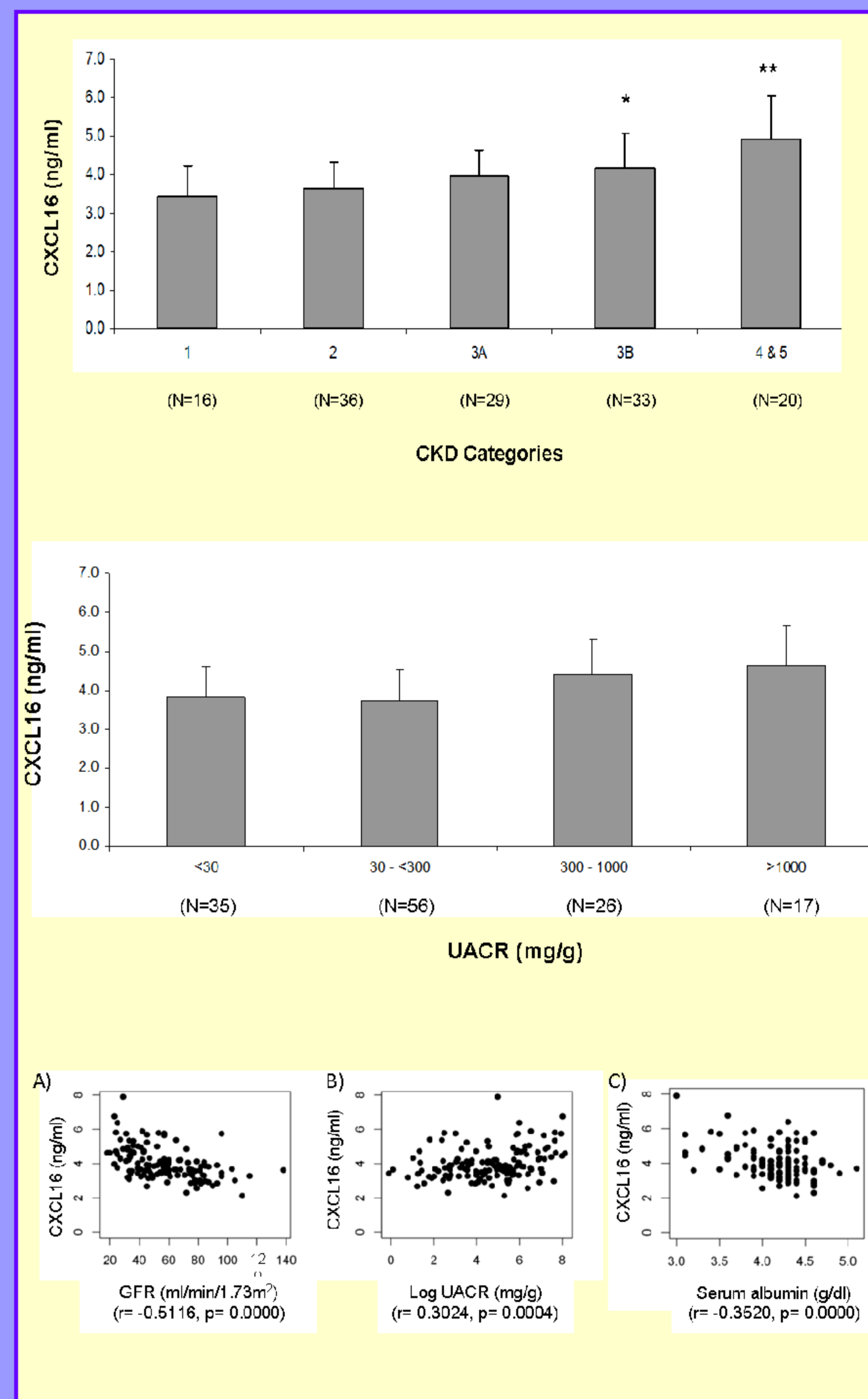
Methods:

This is a cross-sectional analysis of baseline data from patients with 134 diabetic CKD not on dialysis on regular follow-up visits in the diabetic nephropathy clinic. Mean age was 67.9 \pm 13.9 years and the majority was male (92/134, 69%). 40 laboratory parameters potentially related to cardiovascular risk and echocardiogram were prospectively assessed. CKD stage distribution among those patients was 16 (11.9%) stage 1, 36 (26.9%) stage 2, 29 (21.6%) stage 3A, 33 (24.6%) stage 3B and 20 (14.9%) stage 4. Albuminuria 30-300 mg/g Cr was present in 56 patients (41.8%), 300-1000 in 26 (19.4%) and >1000 in 17 patients (12.7%).

Results:

Univariate analysis showed that CXCL16 had a significant positive correlation with age ($r=0.1942$, $p=0.0246$), pulse pressure ($r=0.1865$, $p=0.0310$), urinary albumin/creatinine ratio (UACR) ($r=0.3024$, $p=0.0004$), serum phosphorus ($r=0.2230$, $p=0.0096$), serum alkaline phosphatase ($r=0.2929$, $p=0.0006$) and serum intact PTH ($r=0.3612$, $p=0.0000$). CXCL16 had a significant negative correlation with eGFR ($r=-0.5116$, $p=0.0000$), serum albumin ($r=-0.3520$, $p=0.0000$), diastolic blood pressure ($r=-0.2089$, $p=0.0154$), hemoglobin ($r=-0.3017$, $p=0.0004$), serum carbon dioxide (CO $_2$) ($r=-0.1911$, $p=0.0314$), serum calcium ($r=-0.2284$, $p=0.0079$), serum total iron binding capacity (TIBC) ($r=-0.2399$, $p=0.0052$), serum 1,25 (OH) $_2$ D ($r=-0.2172$, $p=0.0433$) and serum folic acid ($r=-0.1992$, $p=0.0285$).

Multivariate analysis revealed that eGFR ($p=0.0000$) and serum albumin ($p=0.0020$) had an independent and significant negative correlation with plasma CXCL16, while UACR ($p=0.0016$) had significant positive correlation with plasma CXCL16. The best obtained r^2 was 0.30.



Conclusions:

1. Decreased eGFR, serum albumin and UACR are independent predictors of circulating CXCL16 levels.
2. Plasma CXCL16 was not associated with CVD in multivariate analysis.
3. The strong association between eGFR and CXCL16 levels may underlie the disparate observations regarding the relationship between CXCL16 and CVD or outcomes.

