The Importance of Serum CXCL-16 Levels in Patients with Grade III-V Chronic Renal Failure

Hilmi umut ÜNAL¹, Yasemin Gülcan Kurt², Mahmut GÖK¹, Hakkı ÇETİNKAYA¹, Murat KARAMAN ¹, Tayfun EYİLETEN ¹, Abdulgaffar VURAL ¹, Yusuf OĞUZ¹, Mahmut İlker YILMAZ¹

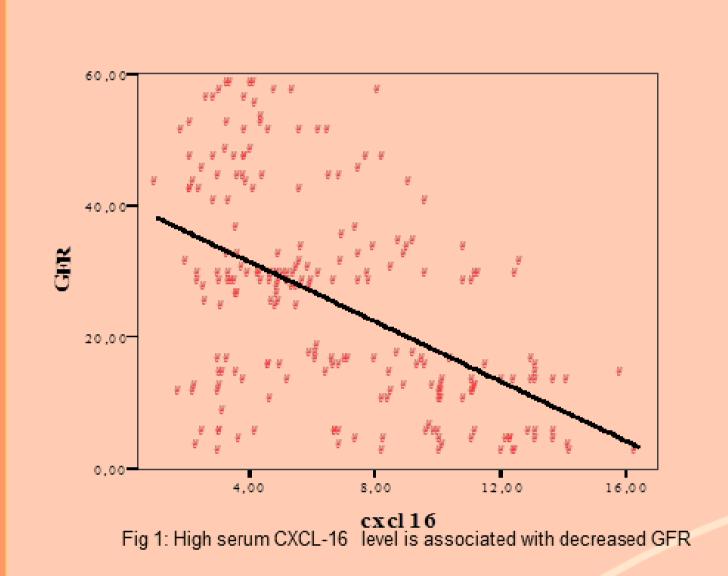
- 1- Department of Nephrology, Gulhane Military Medical Academy, School of Medicine, Ankara, Turkey
- 2- Department of Biochemistry, Gulhane Military Medical Academy, School of Medicine, Ankara, Turkey

Background

CXCL16 functions as a scavenger receptor, which is synthesised in plasmacytoid dendritic cell as a transmembrane molecule, playing a prominent role in the pathogenesis of atherosclerosis (1,2). In addition to its role in atherosclerotic vascular diseases, animal studies indicate, blocking CXCL16 attenuated monocyte/macrophage infiltration and glomerular injury, deletion of CXCL16 attenuated renal fibrosis (3,4). These findings implicate CXCL16 to play an considerable role in the onset and progression of kidney disease. However there are limited studies evaluating the levels of CXCL-16 in patients with chronic renal failure. We aimed to determine the serum level of CXCL-16 in patients with chronic renal disease and to highlighten the relation between CXCL-16 and hsCRP and glomerular filtration rate.

Methods

222 patients with chronic renal disease were included in the study. The patients were devided into 3 groups according to glomerular filtration rate (GFR) in accordance with K/DOQI guideline. 73 patients were grade 3, 73 patients were grade 4 and 76 patients were grade 5 choronic renal failure. Venous blood samples were taken from all individuals included in the study in order to study the detailed metabolic panel, as well as CXCL-16 and hsCRP. Patients with active glomerulonephritis or tubulointerstitial nephritis, heart failure, and hepatic disease, patients who use immunosuppressive or cytotoxic drugs and blockers of reninangiotensin system and smokers were exluded from the study





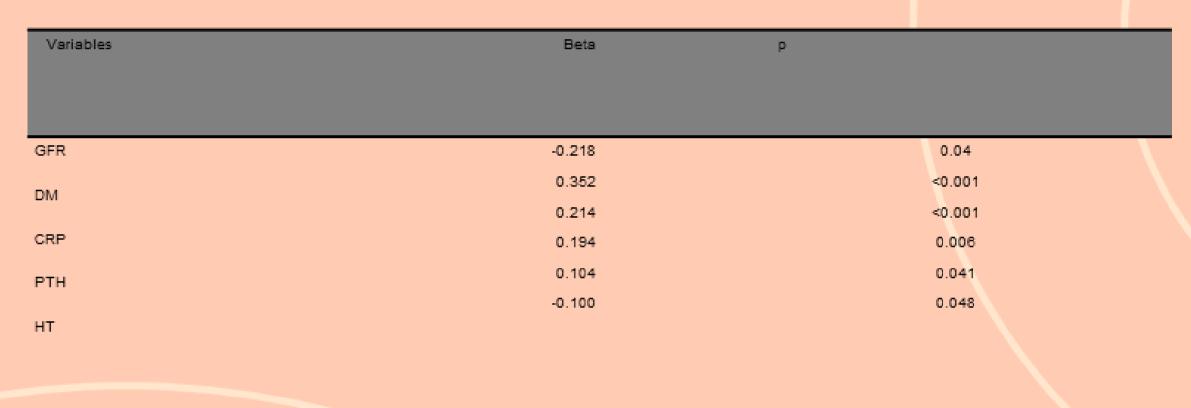


Fig 2: Multiple stepwise regression analysis showing variables independently associated with the serum evel of soluble CXCL16

Results

There was a positive correlation between the grade of renal failure and CXCL-16 and negative correlation between GFR and CXCL-16 (r=-0.457, p<0.001). Moreover hsCRP had positive correlation with grade of renal failure. Moreover there was a negative correlation between hsCRP and GFR. Endothelial function was impaired as parallel to CRD progression and hsCRP values increased as a sign of this positive correlation (r = -0,499, p <0.001). There was a positive correlation between CXCL-16 and hsCRP (r = 0.359 p <0.001). Decreased GFR, increased PTH and hsCRP levels and presence of DM and HT were associated with serum CXCL-16 elevation in multipl regression analysis.

The results indicated that decresed GFR levels were associated with increased hsCRP and CXCL-16 in choronic renal disese. It is concluded that this chemokine which has relation with Framingham risk factors, plays important role in progression of renal disease and development of complications

Conclusions

The previous study by Lin et al. indicated that plasma CXCL16 levels were positively associated with adiponectin, serum phosphate, ESR and uric acid (all p < 0.05) and correlated negatively with HDL-c (p < 0.05) and eGFR (p < 0.001) (5). Gutwein et al. indicated in kidney biopsies of patients with membranous nephropathy, increased glomerular CXCL16 expression was accompanied by high levels of oxidized low-density lipoprotein (6).

These studies suggest that inhibition of CXCL16 could constitute a novel therapeutic approach for chronic kidney disease

References:

1- A. Krug, S. Rothenfusser, V. Hornung, et al., "Identification of CpG oligonucleotide sequences with high induction of IFNα/β in plasmacytoid dendritic cells.," European Journal of Immunology, vol. 31, no. 7, pp. 2154–2163, 2001.

2-T. Shimaoka, N. Kume, M. Minami et al., "Molecular cloning of a novel scavenger receptor for oxidized low density lipoprotein, SR-PSOX, on macrophages," The Journal of Biological Chemistry, vol. 275, no. 52, pp. 40663–40666, 2000.

3-Chen G, Lin SC, Chen J, He L, Dong F, Xu J, Han S, Du J, Entman ML, Wang Y. CXCL16 recruits bone marrow-derived fibroblast precursors in renal fibrosis. J Am Soc Nephrol. 2011 Oct;22(10):1876-86. 4-Garcia GE, Truong LD, Li P, Zhang P, Johnson RJ, Wilson CB, Feng L. Inhibition of CXCL16 attenuates inflammatory and progressive phases of anti-glomerular basement membrane antibody-associated glomerulonephritis. Am J Pathol. 2007 May;170(5):1485-96

5-Lin Z, Gong Q, Zhou Z, Zhang W, Liao Ś, Liu Y, Yan X, Pan X, Lin S, Li X. Increased plasma CXCL-16 levels in patients with chronic kidney diseases. Eur J Clin Invest. 41 (8), 836–845, 2011 6-Gutwein P, Abdel-Bakky MS, Schramme A, Doberstein K, Kämpfer-Kolb N, Amann K, Hauser IA, Obermüller N, Bartel C, Abdel-Aziz AA, El Sayed el SM, Pfeilschifter J. CXCL16 is expressed in podocytes and acts as a scavenger receptor for oxidized low-density lipoprotein. Am J Pathol. 2009 Jun;174(6):2061-72.





