

Serum Level Evaluation of Interleukin-17F and CXCL5 in Patients with Chronic Kidney Disease.

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Abstract

Chronic Kidney Disease (CKD) is defined as defects of kidney structure or function, start for more than 3 months, lead to implications for health. [1].

In this study, included 152 of the samples (94 patients with CKD and 58 healthy), chronic kidney disease cases in stage before ESRD were diagnosed by specialized doctors. The purpose of this study to review of the impact of various inflammation factors, including interleukin 17F (IL-17F), and CXCL5 which may influence on the augmentation of chronic kidney insufficiency.

The serum levels of IL-17F and CXCL5 were determined by using ELISA technique. The results demonstrated that significantly ($p < 0.0001$) Increased of IL-17F and CXCL5 serum level in CKD group than control due to their pro inflammatory role.

Keywords: Chronic Kidney Disease, CKD, IL-17F, CXCL5.

Introduction:

Chronic kidney disease (CKD) is a public health worldwide problem [2]. There have been increasing cases in Asian countries over the past years [3-4]. CKD have relation with mortality increase, the quality of life impaired, and also CKD is costly healthcare problem [5-6]. If the condition remains untreated, this leads to complications that end with dialysis or kidney transplantation [7-8].

T-helper 17 cells produce the cytokine Interleukins -17F (IL-17F) that cause organ injury due to stimulation of the inflammation, as well act on resident cells to produce of pro-inflammatory cytokines, that lead to enhance infiltration of neutrophils to influenced organ and prompt inflammation and injury in this organ for example kidney [9-10].

IL-17F prompted release of the chemokines (proinflammatory proteins act as activators of leukocytes), CXCL5 and CXCL1 in kidney cells, in turn enrolled destructive neutrophils [11-12].

Chemokines are part of the family of cytokine lead to cell activation, migration and organ damage [13]. There is at least (50) structurally linked chemokines have been revealed thus far, and they can be categorized into four subfamilies. An additional 20 receptors have been identified. On binding to their cell receptors, chemokine C-C motif ligands signal leukocyte recruitment and activation leading to tissue inflammation [14]. Extensive literature has delineated the essential role of CCLs in dialysis patients [15], vascular damage [16-17], and transplant pathology [18].

Finally, the majorities of chemokines shares multiple cell receptors and have promiscuous functions ensuring robust inflammatory responses [12]. however, the chemokines C-X-C motif ligand (CXCL) mainly associates with neutrophil activation and recruitment [19].

Procedure

Five ml of a venous blood sample was collected from all patient and control groups, blood serum isolated using centrifugation at 3000 rpm for 10 min, then tubes were sited in a cool-box under sterilized condition and kept in the freezer at (-20°C) until further processing.

Serum levels of IL-17F, and CXCL5 were determined by a commercially available Enzyme-linked immune sorbent assay (ELISA), (Biotechne, USA).

Statistical analysis

Analysis of data was carried out using the available statistical package of SPSS-27 (Statistical Packages for Social Sciences- version 27). The significance of differing means (quantitative data) has been tested using Students-t-test to differentiate between two independent means or Paired-t-test for paired observation differences (or two dependent means). The P value was considered statistically significant less than 0.05.

Results and Discussion:

The results showed that serum level of IL-17F was significantly increased ($P \leq 0.0001$) in CKD group (823.2126 ± 299.5080 pg/ml) as compared with the healthy control group (71.5329 ± 40.1597). Table 1

The results of the current study showed a significant increase in the level of the IL-17F in people with CKD comparing with control group. These results agree with previous study [20].

IL-17F produced by Th17 cells stimulates inflammation through directly causing tissue damage and augmenting secretion of pro-inflammatory cytokines and chemokines via resident cells. These results in augmented infiltration of leukocytes, in particular neutrophils, to the affected tissue where they induce organ inflammation and injury [21].

The serum level of CXCL5 was significantly increased ($P \leq 0.0001$) in CKD group (1094.637 ± 347.352 pg/ml) as compared with the healthy control group (183.360 ± 107.756). Table 1

T cell-derived IL-17F drives renal tissue injury in a non-redundant function in acute crescentic glomerulonephritis and in the chronic model of pristane induced systemic lupus through induction of the chemokines CXCL5 and CXCL1 in resident kidney cells, once more by recruiting tissue destructive neutrophils. [22], This results agree with Previous study [23].

Table 1-Mean serum levels (pg/ml) of IL-17F and CXCL5 in study samples

	CKD Patients	Healthy controls	P value
CXCL5 Concentration	1094.637 ± 347.35 (541.85-2526.65)	183.36 ± 107.76 (65.95-458.19)	0.0001#
IL-17F Concentration	823.2126 ± 299.508 (32.955-1320.32)	71.533 ± 40.16 (18.48-140.51)	0.0001#

#Significant difference between two independent means using Students-t-test at 0.05 level.

CONCLUSION

IL-17F and CXCL5 play an essential role as pro-inflammatory cytokines in Chronic Kidney Disease patients and development disease.

References:

- 1- Agarwal, S.K. and Srivastava, R.K. (2013). Definition and classification of CKD. *Nephron ClinPract.*, 3(1):19-62.
- 2- Stewart, J.H.; McCredie, M.R. and Williams, S.M. (2006). Geographic, ethnic, age-related and temporal variation in the incidence of end-stage renal disease. *Nephrol Dial Transplant.*, 21(8): 2178-2183.
- 3- Sakhuja, V. and Sud, K. (2003). End-stage renal disease in India and Pakistan: burden of disease and management issues. *Kidney Int Suppl.*, (83): 115-118.
- 4- Khan, S.; Hussain ,T.; Salahuddin, N. and Mehreen, S. (2016). Risk Factors of End Stage Renal Disease. *Open Access Maced J Med Sci.*, 4(3): 381-387.
- 5- Khan, S.; Hussain, T.; Azam, H. and Salahuddin, N. (2015). Statistical Study of Risk Factors of End Stage Renal Failure . *Open Access Maced J Med Sci.*, 3(1): 189-194.
- 6- Alam, A.; Amanullah, F.; Baig-Ansari, N.; Lotia-Farrukh, I and Khan, F.S. (2014). Prevalence and risk factors of kidney disease in urban Karachi: baseline findings from a community cohort study. *BMC Res Notes.*, 7: 179.
- 7- Ali Jaffar Naqvi, S. (2000). Nephrology services in Pakistan. *Nephrol Dial Transplant.*, 15(6): 769-771.
- 8- Jafar, T.H. (2006). 71% of patients with newly diagnosed chronic kidney disease progressed to renal replacement therapy or death within 3 years. *Evid Based Med.*, 11(4): 118.
- 9- Zhao, M.; Tan, Y.; Peng, Q.; Huang, C.; Guo, Y.; Liang, G.; Zhu, B.; Huang, Y.; Liu, A.; Wang, Z. and et al.(2018). IL6/STAT3 pathway induced deficiency of RFX1 contributes to Th17dependent autoimmune diseases via epigenetic regulation. *Nat Commun.*, 9: 583.
- 10- JALIL, A.T., DILFY, S.H., KAREVSKIY, A. and NAJAH, N., 2020. Viral Hepatitis in Dhi-Qar Province: Demographics and Hematological Characteristics of Patients. *International Journal of Pharmaceutical Research*, 12(1).
- 11- Paust, H.J.; Riede, J.H.; Krohn, S.; Turner, J.E.; Kluger, M.A.; Steinmetz, O.M.; Krebs, C.F.; Stahl, R.A.K. and Panzer, U.(2016). TRANSLATIONAL IMMUNOLOGY IN KIDNEY DISEASE. *ISN NEXUS SYMPOSIUM.*, P40.
- 12- Jalil, A.T. and Karevskiy, A., 2020. The Cervical Cancer (CC) Epidemiology and Human Papillomavirus (HPV) in the Middle East. *International Journal of Environment, Engineering & Education*, 2(2), pp.7-12.
- 13- Moser B, Willimann K. Chemokines(2004). role in inflammation and immune surveillance. *Ann Rheum Dis.*, (63) 2:84–9.
- 14- Murdoch C, Finn A.(2000).Chemokine receptors and their role in inflammation and infectious diseases. *Blood.*,95:3032–43.
- 15- Chung, ACK. and Lan, H.Y.(2011). Chemokines in renal injury. *J Am Soc Nephrol.*, 22:802–9.
- 16- Zernecke, A. and Weber, C. (2010). Chemokines in the vascular inflammatory response of atherosclerosis. *Cardiovasc Res.*, 86:192–201.
- 17- Sozzani, S.; Del Prete, A.; Bonecchi, R. and Locati, M.(2015). Chemokines as effector and target molecules in vascular biology. *Cardiovasc Res.*, 107:364–72.
- 18- Hancock, W.W. (2002). Chemokines and transplant immunobiology. *J Am Soc Nephrol.*,13:821–4.

- 19- Bachelierie, F.; Ben-Baruch, A.; Burkhardt, AM.; Combadiere, C.; Farber, J.M.; Graham, G.J. and et al. (2013). International Union of Basic and Clinical Pharmacology. LXXXIX. Update on the extended family of chemokine receptors and introducing a new nomenclature for atypical chemokine receptors. *Pharmacol Rev.*, 66(1):1–79.
- 20- Asaal, A-G.S.; Mohammed, A-D. S. and Nihad Kh. T. (2020). Immunological role of TLR-7, IL-17A and IL-10 In a Sample of Iraqi Chronic Renal Failure Patients. *Medico-legal*. 20(1).
- 21- Jan-E. T.; Hans-J. P.; Oliver M. S.; and Ulf P. (2010) The Th17 immune response in renal inflammation. *International Society of Nephrology*. 77: 1070–1075.
- 22- Jan-H. R.; Jan-E. T. and Ulf P. (2021). T helper cell trafficking in autoimmune kidney diseases. *Cell and Tissue Research*. 27: 3666–3677.
- 23- Jan-H. R.; Hans-J. P.; Sonja K.; Jan-E. T.; Malte, A.; Kluger, O. M.; Steinmetz, z.; Christian, F.; Krebs, A.K. and Ulf, P. (2016). IL-17F Promotes Tissue Injury in Autoimmune Kidney Diseases. *J Am Soc Nephrol* 27: 3666–3677.