The Role of CXCR3 in Cardiovascular Disease Patients in Thi-Qar Province, Iraq

Eltfat T. Attia[1], Ali N. Salman[2*]

Abstract

The present study was carried out in the Labs of Al-Hussein Teaching Hospital in Nassiriya city, during period from December 2020 to end July of 2021. The immune status investigates for patients with cardiovascular diseases by measuring the levels of chemokine receptor (CXCR3) in serum using a technique enzyme-linked immune Sorbent adsorptive (ELISA). The study included 65 subjects with (38) mele, (27) female and (25) were healthy control. The statistical analysis showed that a high significant increase (P ≤0.001) in serum the rate of concentration of CXCR3 in patients (1.15±3.143pg/ml) compared to the control group (1.68±5.025pg/ml) with significant difference (0.001). These results revealed that the excessive presence of chemokines might play a role in cardiovascular diseases in Nassryain population.

Key Words: CXCR3, Cardiovascular Disease, CXC Chemokine.

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Introduction

The CXC chemokines, CXCL-9, -10, -11, and the CC chemokine CCL21, activate CXC chemokine receptor 3 (CXCR3), a cell-surface G protein-coupled receptor expressed mainly by Th1 cells, cytotoxic T (Tc) cells and NK cells that have a key role in immunity and inflammation. However, CXCR3 is also expressed by vascular smooth muscle and endothelial cells, and appears to be important in controlling physiological vascular function. In the last decade, evidence from pre-clinical and clinical studies has revealed the participation of CXCR3 and its ligands in multiple cardiovascular diseases (CVDs) of different aetiologies including atherosclerosis, hypertension, cardiac hypertrophy and heart failure. CXCR3 ligands have also proven to be valid biomarkers for the development of heart failure and left ventricular dysfunction, suggesting an underlining pathophysiological relation between levels of these chemokines and the development of adverse cardiac remodelling. The observation that several of the above-mentioned chemokines exert biological actions independent of CXCR3 provides both opportunities and challenges for developing effective drug strategies(1). The chemokine receptor CXCR3 and associated CXC chemokines have been extensively investigated in several inflammatory and autoimmune diseases as well as in tumor development. Recent studies have indicated the role of these chemokines also in cardiovascular diseases. We aimed to present current knowledge regarding the role of CXCR3-binding chemokines in the pathogenesis of atherosclerosis and during acute myocardial infarction(3). Atherosclerosis is a chronic inflammatory disease, with immune cells and their effector molecules initiating and maintaining the progression of atherosclerotic lesion formation, accompanying and also precipitating acute coronary events and the following reparatory processes (12).

Corresponding author: Ali N. Salman
Address: [1,2*]Department of Biology, Faculty of Education for Pure Sciences, University of Thi-Qar, Iraq.
[2*]E-mail: dr.ali-n@utq.edu.iq
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Chemotactic cytokines, or so-called chemokines have been shown to facilitate leukocyte migration during inflammatory responses to various stimuli, including their recruitment to the sites of atherosclerotic lesions[6]. The present review focuses on the role of the IFN-γ inducible chemokines and their receptor CXCR3 in the development of atherosclerosis and consequent coronary artery disease. Possible clinical implications of the presented findings are not entirely clear, but the currently available clinical studies suggest that this might be a promising area of intervention in the future of cardiovascular therapy and prevention [15]. CXCR3 is a 7-transmembrane spanning (7-TMS) G-protein-coupled cell surface receptor that allows functional selectivity on tissue, receptor as well as ligand levels [2]. It binds three inflammatory chemokines CXCL9, CXCL10, and CXCL11 [7, 10].

Material and Methods

This study was performed on 80 Iraqi patients with cardiovascular diseases included atherosclerosis, myocardial infraction, heart attack patients, in Al-Hussein Teaching Hospital in the period from the beginning of December 2020 to end July of 2021.Blood samples were collected. Two milliliters were placed in a gel tube and allowed to clot, then serum was separated by centrifugation at 5000 rpm for 5 minutes. The serum was stored at -20 C° freezing. The current study sample was divided according to gender, type of disease, and the relationship between them. The three cardiovascular diseases under study were distributed between the two sexes (females and males). ELISA (technique enzyme-linked immune Sorbent adsorptive) kit are employing the quantitative sandwich, were based on similar principle according to the Elabscience company (China, E–EL- H0854).

Statistical analysis

Data were expressed as mean ± standard deviation (SD) or median (interquintile range). Differences between groups were tested with the Student's t-test. The values of P < 0.001 were considered significant.

Result

Table (1): shows the value of the numbers of the two groups, patients and healthy controls by gender, as the results showed that the current study sample was divided according to gender, and the relationship between them. cardiovascular diseases under study were distributed between the two sexes (females and males). The results of the current study showed that the percentage of males with cardiovascular diseases is greater than the percentage of females, as their percentage was 58.75%, and they numbered 47, while the percentage of females was 41.25 %, numbering 33. As shown in the table (1).

Table 1. Comparison between the two study groups according gender

Gender	Patients		Control		P. Value
Male	N.	%	N.	%	
	47	58.75	13	52.0	**0.597**
Female	N.	%	N.	%	
	33	41.25	12	48.0	
Total	N.	%	N.	%	
	80	100.0	25	100.0	

Table (2) The current study showed a decrease in the level of the chemokines receptor CXCR3 in patients with CVDs (1.15 ± 3.143) pg/ml compared with the healthy group (1.68 ± 5.025) pg/ml with a significant difference with a statistically significant high (P < 0.001).

Table 2. Comparison of the levels of the chemical kinetics receptor CXCR3 between the two study groups

Parameter	Groups	n.	Mean ± SD	P. Value
CXCR3	Patient	65	1.15±3.143	
	Control	25	1.68±5.025	**0.001** P<

The study sample under study was divided according to the disease and age groups, and the relationship between them. cardiovascular diseases were studied Our results in this study showed that the largest percentage of people with cardiovascular diseases was in the age group 51-75, which represented 53.25% (35patients) .As for the study of heart disease, our study under consideration showed that the 51-75 age group itself constituted the largest proportion in terms of the number of patients. Table (3) explains all of the above.

Table (3): shows the value of the numbers of the three groups, patients and healthy controls by age group, as the results showed that the age group (51-75) was the most affected among the other groups. with a significant difference with a statistically significant high (P < 0.001).

Table 3. Comparison of serum(CXCR3) concentration (pg/ml)in the group of patients according to age groups

Parameter	Age groups	Patients		control		P. Value
		%	No.	%	No.	
CXCR3	25-50 year	**35.4**	**23**	**32**	**8**	**P. < 0.001**
	51-75 year	**53.8**	**35**	**48**	**12**	
	More75 year	**10.8**	**7**	**20**	**5**	

Discussion

Inflammatory in cardiovascular disease involve intense chemokine signaling from the forming of the atherosclerotic plaque to all phases of acute coronary events and infarct healing [14].) IFN-γ inducible chemokines CXCL9, CXCL10, and CXCL11 attract activated T cells through CXCR3 receptor to the site of infarction. Modulation of their action might prevent the excessive recruitment of leukocytes to sites of inflammation and consequently influence the clinical outcome of the disease [5]. Chemokine levels have a short half-life and may have high intraindividual variability [9]. this results in difficulties in estimating the best sampling time and may generate conflicting clinical results. This study agreed with[11]. In a study in mice, pharmacological inhibition of CXCR3 leads to decreased atherosclerotic plaque formation, which is accompanied by decreased activation of Th1 cells and increased migration of regulatory T lymphocytes to the lesions, mice showed a decrease in atherosclerosis with increased numbers of atherosclerotic cells. and Treg cell activity. Furthermore, antibody-mediated inhibition of CXCL10 resulted in a more stable plaque phenotype. This study agreed with another 2010 study that an increased systemic inflammatory activity is present in patients with coronary artery disease, which is characterized by an increased proportion of IFN-γ-positive Th1 lymphocytes. In patients with stable angina pectoris, enhanced systemic expression of CXCL9, CXCL10, and CXCR3 can be observed. While lower levels of these chemokines and CXCR3 were found in the peripheral cells of patients with acute coronary syndrome, indicating the sequestration of CXCR-positive cells circulating from the blood to the infarct site by intense in situ release of these chemokines[3]. This study was in agreement with[16].which showed lower levels of CXCL11 in plasma in patients with stable and unstable angina pectoris compared to healthy controls. Thus CXCL11 may have a protective effect in unstable angina by stabilizing atherosclerotic plaque. He found that other anti-inflammatory molecules known to have a protective effect in cardiovascular disease affect T-cell trafficking through the chemical system. Adiponectin has been shown to inhibit CXCR3 production in macrophages, while heparin competes to bind to CXCL9, CXCL10, and CXCL11 on endothelial cells[8]. A significant association was found between an increase in serum CXCL10 and the risk of coronary heart disease. Higher levels of CXCL10 have also been found to be independently associated with laboratory-confirmed CHD risk markers such as acute phase proteins and inflammatory cytokines[13].

This study was consistent with[17] who explained in his study that advancing age is an influencing factor on cardiovascular diseases, and the risk of atherosclerosis increases with age, and atherosclerosis does not appear clinically until middle age or thereafter. When arterial lesions lead to injury to the organ. The results of this study are in agreement with the study [18] which showed that the incidence of myocardial infarction increases fivefold among the age group ranging from 40 to 60 years. The risk of cardiovascular disease increases significantly with age, as there is an accumulation of fat, high blood pressure, smoking, obesity and diabetes that increase the risk of infection. The presence of chemokines in blood is a prominent feature of the post-infarction period as it plays an important role in regulating the infiltration and activity of white blood cells and modulating angiogenesis and fibrous tissue infarction. CXCL10 may act to prevent early wound angiogenesis and deposition of fibrous tissue in the infarction, until clear Infected heart muscle from dead cells and debris. Cellular behavior in vascular tissues is directed by chemical kinetics. Various types of kinetics and their receptors have been described as being involved in vascular remodeling. CXCL10 contributes to the pathophysiology of cardiovascular diseases such as atherosclerosis, aneurysm, and thrombosis.

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