



Estimation of 6Ckine and Chemokine Receptor Type 7 With Some Biomarkers in Type 2 Diabetes Mellitus Patients in Ramadi City-Iraq

Ahmed Abdulkader Humadi¹, Othman Rashid Al Samarrai^{1*} and Khalid F. Al-Rawi²

¹Department of Chemistry, College of Education, University of Samarra, Samarra, Iraq.

²Department of Chemistry, College of Science, University of Anbar, Ramadi, Iraq.



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Abstract

Type 2 Diabetes Mellitus (T₂DM) it is a complex disease associated with metabolic disorders. The main aim of this study was to accurately estimate the concentration of Chemokine (6Ckine) and Chemokine Receptor Type 7 (CCR7) with some biomarkers in blood serum of T₂DM patients and compare it with healthy control. Identical in gender and age ranged from (40-70) years, 60 diabetics and 30 healthy controls participated in this study of 6Ckine and CCR7 serum concentration was estimated by Enzyme Linked Immune Sorbent Assay (ELISA) technique. An 6Ckine and CCR7 were no different between patients and healthy control. Oxidized Low Density Lipoprotein (Ox-LDL) showed increased significantly in T₂DM patients compared to healthy control, and insulin shows decrease significantly in T₂DM patients compared to healthy control, and each for age and Body Mass Index (BMI) also increase significant between T₂DM patients and healthy control. The conclusion of this study showed an increase in the level of Ox-LDL in patients compare with healthy control, no different between patients and healthy control in levels of both 6Ckine and Chemokine Receptor Type 7, decrease in insulin level in patients compare with healthy control.

Keywords: 6Ckine, Chemokine Receptor Type 7 (CCR7), Type 2 Diabetes Mellitus (T₂DM), Oxidized low-density lipoprotein (Ox-LDL), Body Mass Index (BMI)

1. Introduction

Diabetes Mellitus (DM) that occurs when the pancreas does not produce insulin effectively, and it may be an acquired or hereditary deficiency, and treatment must be continued it requires daily attention to diet, lifestyle and permanent use for treatment, and constant monitoring of level blood sugar throughout life with anxiety and depression [1,2].

Conventionally, complications of high blood sugar are categorized into two components complications of microvascular and large blood vessels, complications of small vessels are represented by neuropathy, retinopathy and nephropathy, while large vessels are represented by peripheral arterial disorder, stroke and coronary artery disease [3]. There are several types of diabetes and there are two common sub-types, Type 1 Diabetes Mellitus (T₁DM) and Type 2 Diabetes Mellitus (T₂DM), followed by other types including gestational diabetes and other types for other reasons [4].

Type 2 Diabetes Mellitus (T₂DM) it is one of the most common causes of disease causes, either

because of insulin resistance or weak insulin secretion, or both, and it is considered a global epidemic [5]. T₂DM it represents about 95% among the other types of people with diabetes and it is considered one of the most common types and is described by insulin resistance in the surrounding tissues or by low insulin sensitivity, which means an insufficient response to insulin [6].

Many diseases, including type 2 diabetes, chemicals and their receptors play an important role in regulating inflammatory events [7]. In another study, chemicals play an important and clear role in the development of disorders related to obesity, including type 2 diabetes, because they play a role in pathophysiological and physiological conditions as a crucial immune mediator [8]. The risk factors for type 2 diabetes increase and the risk of developing the disease increases when the chemokine concentration is above average [9].

Cytokines are shows its important role in inflammatory and immune responses [10]. Chemokines is a member of the family of cytokines and is expressed by adipocytes and primary fat cells, and the sequences of macrophages derived

*Corresponding author e-mail: othman.samarrai@uosamarra.edu.iq; (Othman Rashid Al Samarrai).

Receive Date: 26 May 2021, Revise Date: 02 June 2021, Accept Date: 08 June 2021

DOI: [10.21608/ejchem.2021.77687.3792](https://doi.org/10.21608/ejchem.2021.77687.3792)

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from the bone marrow to the physical adipose tissue appear. They participate in the development of insulin resistance [11,12]. Chemokines are highly fundamental proteins containing of (70-125) amino acids with molecular masses extending from (6-14) kD, chemokines classification is four subfamilies (C, CC, CXC, CX3C) created on the comparative position of conserved cysteine remains in the N-terminal [13].

Chemokine (6Ckine) also referred to as CC-ligand 21/ or secondary lymphoid-tissue chemokine (CCL21/SLC) or exodus, 6Ckine is essential articulated in elevated endothelial venules of thymus, lymph nodes, spleen, mucosal tissue and Peyer's patches. It has a high affinity for Chemokine Receptor Type 7 (C-C-Motif Receptor 7(CCR7)), which is included into employing, memory T, CCR7 T cells and natural killer [12].

Chemokine receptors: There are two groups of heptamine-cell surface molecules that bind to chemicals: atypical chemokine receptors (ACKRs) and conventional chemokine receptors (cCKRs) [13].

The CCR7 is a member of the G protein-paired receptor family (GPCR) and by binding to cytokines CCL21 and CCL19 mature stem cells can be activated CCR7. It is expressed mously in memory B cells, C cells. [14]. Main goals of this study were evaluate serum 6Ckine and CCR7 concentrations in T₂DM.

2. Materials and Methods

2.1. Sample collection

The current study included 60 patients with Type 2 Diabetes Mellitus (T₂DM), of both sexes, whose ages ranged between (40-70) years. This study was carried out at the Ramadi Teaching Hospital in Ramadi city- Al Anbar Governorate-Iraq, conducted during in the period from October 2020 to December 2020. After clinical examination by the consultant physicians and after approval from the patients. Blood samples were collected from the patients, the history of treatment and lifestyle has been taken into account. They were compared with 30 healthy controls of both sexes with same ages of patients.

2.2. Blood collection

After 8 hours of fasting, the blood was drawn and left at room temperature for coagulation and for a period of a quarter of an hour, the serum was expelled at 5000 x g and the separated sera were frozen at -20 ° C for future biochemical analysis [15].

2.3. Biochemical parameters analyses

Blood glucose was determined according to enzymatic method [16], by using the glucose kit providing by (Linear, Spain), and the 6Ckine was measured by Enzyme Linked Immune-Sorbent Assay (ELISA) method, the ELISA kit providing by (Elabscience, China), bearing the number EKHU-0184, and CCR7 was measured by ELISA method, the ELISA kit providing by (Elabscience, China), bearing the number EKHU-2156, and Insulin (INS) was measured by (ELISA), the ELISA kit providing by (Elabscience, China), bearing the number EKHU-1751, and Ox-LDL was measured by ELISA method, the ELISA kit providing by (Elabscience, China) bearing the number EKHU-0841.

2.4 Statistical analysis

Using Graph Pad prism version 7.04 and Software Excel 2016, Statistical analysis of the data was done. The descriptive statistics for each parameter consisted of the standard error (SE), the mean and the standard deviation (SD). The T-test was used to compare the chemical variables between patients and control groups at the level of probability ($P \leq 0.05$). The results were interpreted using Median [17].

3. Results

The results in table (1) showed a significant increase ($P \leq 0.05$) in the concentration of Age, BMI, glucose and Ox-LDL in patients compare with healthy control. And showed a significant decrease ($P \leq 0.05$) in the insulin concentration in patients compare with healthy control. 6Ckine and CCR7 were no different between patients and healthy control.

The results in table (2) displayed the interpreted using Median, results showed the levels of 6Ckine, CCR7, insulin and Ox-LDL were higher in patients than healthy control when compared to use. But it was not significant in Mean \pm SD.

Table 1. Age, BMI and concentration of biochemical parameters in the serum of patients with type 2 diabetes mellitus compared to healthy controls

Parameters	Mean \pm SD		P-Value
	Control	Patients	
Age (year)	48.720 \pm 8.085	53.120 \pm 8.991*	0.02
BMI (kg/m ²)	28.204 \pm 3.025	30.831 \pm 5.990*	0.023
Glucose (mg/dl)	82.840 \pm 9.932	185.070 \pm 64.314***	0.0001
6Ckine (ng/ml)	1.366 \pm 0.444	1.236 \pm 0.442	0.196
CCR7 (ng/ml)	1.652 \pm 0.425	1.601 \pm 0.475	0.610
Insulin (μ IU/ml)	6.800 \pm 1.539	5.617 \pm 1.422***	0.001
Ox-LDL (μ g/ml)	2.112 \pm 1.184	2.816 \pm 1.491*	0.036

* This sign means different significant at $P \leq 0.05$.

*** This sign means different significant at $P \leq 0.001$

Table 2. Parameters values between patients and control using Median.

Parameters	Control	Patients
6Ckine	1.191	1.422
CCR7	1.578	1.636
Insulin	5.695	6.529
Ox-LDL	1.887	2.143

4. Discussion

The findings were consistent with the results of one of the studies that found an increase in the value of chemokines in general, as it is possible that chemokine signalling has an important and effective role in the development of atherosclerosis, and that chemokine secretion increases the development of diabetes. It is thought to have a role in the increased production of chemokine, which is known to regulate. When activated, normal T cells are expressed and secreted [18]. And because studies have shown that diabetes is an inflammatory disease and that chemokines are inflammatory factors, therefore we found an increase in its concentration in diabetics compared to healthy people.

The CCR7 is responsible for leading the movement of dendritic cells to the lymph nodes as these cells have an essential job in an onset of the immune response. It was initially described as a strong chemical receptor for white blood cells [19]. It is important for the thymus cells to be identified, as they are known to play a role in immune diseases, and they also have a documented association with lesions related to autoimmune diseases [20].

And because diabetes is an autoimmune disease and dendritic cell is involved in inducing

autoimmune diseases, so we noticed an increase in CCR7 because it is responsible for directing these cells.

Oxidized low-density lipoprotein (Ox-LDL) is formed in the oxidation state of low-density lipoprotein cholesterol (LDL-C) which then leads to the accumulation of foamy cells under the endothelium. And these foam cells in the development of atherosclerotic plaques [21].

Accumulation of multiple risk factors such as hyperglycemia lead to cerebrovascular and cardiovascular complications in diabetic patients. It is generally recognized that T₂DM-associated vascular disease is mainly associated with vascular endothelial injury and endothelial dysfunction, which are the initial steps leading to atherosclerosis. Recently, some studies analyzed the key factors of inflammatory injuries in T₂DM and these factors include oxidized low-density lipoproteins (Ox-LDL). T₂DM associated with high levels of Ox-LDL [22]. Free radicals excess that attack the fats and lead to or cause peroxidation of the lipid molecules are formed in a chain reaction. High blood sugar may be one of these causes. The concentration of OxLDL is an indication of residual and accumulated fat in addition to the traditional lipid tests known to diagnose or predict

cardiovascular risks as well as control and control lipid content in type 2 diabetic patients [23].

5. Conclusion:

This study showed an increase in the concentration of both 6CKine and CCR7 as an inflammatory and atherogenesis and the important role for them in predicting and controlling the disease and possibly in the treatment of type 2 diabetes patients.

Acknowledgments

The authors are thankful for the Head of laboratories in department of Chemistry, College of Education, University of Samarra.

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