The Egyptian Journal of Hospital Medicine (July 2018) Vol. 72 (4), Page 4403-4406

Assessment of Interleukin (8) in Type 2 Diabetes Mellitus

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ABSTRACT

Background: Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Type 2 diabetes (T2D) is characterized by a condition of systemic low-grade inflammation. IL-8 is an important member of the chemokine family of proinflammatory chemotactic cytokines. IL-8 was initially characterized as a potent chemoattractant of neutrophils and was later shown to also activate neutrophils. IL-8 is also known to be a potent promoter of angiogenesis.

Objective: It was the Assessment of Interleukin (8) in Type 2 Diabetes Mellitus.

Patients and Methods: Serum IL 8 level in Type 2 Diabetes Mellitus. 30 patients compared to 30 normal individuals were included in this study.

Results: There was a highly statistical significant difference between all patients and control groups as regard serum IL 8 level (mean of serum IL 8 in patients and control groups were 69.9 ± 20.5 and 5.4 ± 3.3 respectively, p= < 0.001).

Conclusion: Type 2 diabetes mellitus patients showed marked elevation of circulating IL-8 levels which identify subjects with worse inflammatory state and metabolic control and therefore it may be used as a marker for the rate of development of diabeteic complications.

Keywords: Type 2 Diabetes Mellitus, Interleukin-8, CXC chemokine

INTRODUCTION

Diabetes is the most common endocrine disorder, affecting in the year 2013, about 382 million people worldwide and it is estimated that in 2035, over 592 million cases of diabetes will be registered [(1)].

Type 2 diabetes (T2D) is characterized by a condition of systemic low-grade inflammation which represents a key factor for the development of insulin resistance and associated comorbidities, such as non-alcoholic fatty liver disease (NAFLD) and atherosclerosis. Insulin resistance is defined as the impaired ability of target tissues of fat, liver, and muscle to show various metabolic effects of insulin, including glucose uptake [(2)].

Interleuken-8 is a pro-inflammatory polypeptide belonging to the CXC chemokine superfamily, characterized by the presence of two cysteine residues separated by an intervening aminoacid in the first three positions, and is secreted by several cell types, including adipocytes, monocytes / macrophages, T-lymphocytes, endothelial and epidermal cell [(3)].

As a multifunctional chemokine, interleukin-8 has chemoattractant and mitogenic effects on neutrophils as well as on T-cells, vascular smooth muscle cells, vascular endothelial cells and monocytes [(4)].

Among its multiple actions, IL-8 also promotes macrophages infiltration in adipose tissue (AT) inducing local and systemic inflammation and representing, in turn, a potential Link between AT dysfunction and insulin resistance-related conditions [(5)].

Several cross-sectional studies showed that insulin resistance and T2D are associated with higher circulating levels of C-reactive protein (CRP), IL-6 and TNF-α, in addition, the chemokine system, in particular interleukin-8 (IL-8), came more recently into the focus of metabolic inflammation research [(6)].

This study was performed to evaluate circulating plasma IL-8 levels in adult patients with type 2 diabetes mellitus in comparison with non-diabetic subjects.

SUBJECTS AND METHODS

Subjects:

This study was conducted in collaboration between the Clinical Pathology and Internal Medicine department at Al-Hussein University Hospital, Faculty of Medicine, Al-Azhar University. **The study was approved by the Ethics Board of Al-Azhar University.**

All patients were collected from the outpatient clinic and Internal Medicine department at Al-Hussein University Hospital over a period from 15th January 2018 to 5th April 2018, with appropriate consent to participate in this study after explanation to the patients how much it is helpful in diagnosis and treatment and also explaining to them that it is just a blood sample collection. Those subjects were divided into 2 groups: (patients group) and (control group).

Patients group (B) including 30 patients suffering from type 2 diabetes mellitus.

Received:17/5/2018
Accepted:26/6/2018

Control group (A) comprised 30 apparently healthy persons not suffering from DM either clinically or laboratory.

Inclusion criteria

Patients suffering from type 2 diabetes mellitus from the outpatient clinic and Internal Medicine department at Al-Hussein University Hospital (controlled and uncontrolled DM).

Diagnosis was based on:

History of type 2 diabetes mellitus (including drug, family history,age… etc).

Clinical features of marked hyperglycaemia as per American Diabetes Association 2018 criteria, including polyuria, polydipsia, weight loss, sometimes polyphagia and blurred vision … etc.

Lab features of type 2 diabetes mellitus (including FBS,2hrsPP,HbA1C… etc).

Exclusion criteria:

Patients of type 1 diabetes mellitus.

Patients of type 2 diabetes mellitus with diabetic coma.

Samples and methods

Full history and clinical examination. Eight ml venous blood were withdrawn from all participants of the study and divided into four portions: the first portion (two ml) was put in EDTA tube for HbA1C. The second portion (two ml) was put in plain tube for routine biochemical tests.The third portion(1ml) was used on flouride for blood glucose(fasting – 2hrsPP).These tests (FBS, 2hrsPP, HbA1C and routine biochemical tests) were done using Cobas c311& Intejra analyzer (Roche Diagnostics).The fourth portion (three ml) was put in plain tube and left to clot at room tempreture for 2 hours then centrifuged and the serum was separated and stored at -20 □C until assessed for IL-8 using enzyme linked immunosorbent assay (ELISA), commercial kits purchased from R & D systems, Inc. USA.

Statistical analysis

All results were analyzed using Statistical package for social science (SPSS V.15, IBM Corp. U.S.A).

Descriptive statistics was used for quantitative data analysis: They were; Mean ±SD while Qualitative data were expressed as frequency and percentage.

Wilcoxon rank sum test: as data related to IL-8 were skewed, we used this non parametric test for analysis.

Pearson correlation coefficient was used to check for correlation between two quantitative parametric data.

For all analysis, a two-tailed test was used and $p < 0.05$ was considered statistically significant.

RESULTS

As regard to serum IL 8 level, there was a statistically highly statistical significant difference (p-value < 0.001) between studied groups as to regard IL-8, table (1).

Results show a highly statistical significant (p-value < 0.001) positive correlation between IL-8 and (FBS, PPBS and Hb A1C) in patients group while there was a statistically significant (p-value < 0.05) Negative correlation between IL-8 and age in patients group, table (2).

Table (1): Comparison between studied groups as regard IL-8.

Groups		Patients Group (N = 30)	Control Group (N = 30)	T-Test	
				T	p-value
IL-8 (pg/ml)	**Mean**	69.9	5.4	16.9	**< 0.001**
	±SD	20.5	3.3		

Table (2): Correlation study between serum IL-8 and other studied parameters in patients group.

Groups / Parameters	Patients group	
	(r)	p-value
IL-8 vs age	- 0.4	**0.01**
IL-8 vs FBS	0.8	**< 0.001**
IL-8 vs PPBS	0.7	**< 0.001**
IL-8 vs creatinine	0.2	0.1
IL-8 vs urea	0.03	0.8
IL-8 vs AST	0.06	0.7
IL-8 vs ALT	0.01	0.9
IL-8 vs HbA1C	0.9	**< 0.001**

DISCUSSION

Diabetes mellitus is a complex of syndromes characterized metabolically by hyperglycemia and altered glucose metabolism and associated pathologically with specific microvascular complications, macrovascular disease secondary to accelerated atherosclerosis, and various other complications, including neuropathy, retinopathy, nephropathy, complicated pregnancy, and an increased susceptibility to infection [7].

IL-8 is considered as an important cytokine in the inflammatory process, it is a member of the CXC chemokine family that has potent chemoattractant activity for leukocytes and potent promoters for angiogenesis. It's main sources are

several cell types, including adipocytes, monocytes / macrophages, T-lymphocytes, endothelial and epidermal cell [8].

Several cross-sectional studies showed that insulin resistance and T2D are associated with higher circulating levels of C-reactive protein (CRP), IL-6 and TNF-α, in addition, the chemokine system, in particular interleukin-8 (IL-8), came more recently into the focus of metabolic inflammation research [9].

The present study was conducted on 60 subjects, 30 type 2 diabetics and 30 healthy control persons (not affected by any comorbidities and not treated with any medications at the time of study recruitment).The diabetics were selected randomly of both insulin and noninsulin treatment, from outpatient clinic and internal medicine department at Al Hussein University Hospital, from January 2018 to April 2018.

This case control study aimed at evaluating circulating plasma IL-8 levels in adult patients with type 2 diabetes mellitus in comparison with non-diabetic subjects. The diabetic patients were suffering from type 2 diabetes mellitus for years with (mean 8.9±6.9 years). They have bad control and management for the disease with FBS (main 207.5±89.2 mg/dL), PPS (main344.6±135.3 mg/dL) and the HbA1C test for them (main 6.9± 1.5%).

This study reported that the serum IL-8 concentration in type II diabetic patients was markedly increased in comparison with healthy subjects. IL-8 showed highly statistical significant (p-value < 0.001) Positive correlation between IL-8 and (FBS, PPBS and HbA1C) in patients group.

This result was in agreement with that of ***Cimini*** [10]. They reported that the serum concentration of IL-8 was (mean ± SD: 69.27 ± 112.83 pg/mL vs. 16.03 ± 24.27 pg/mL, p < 0.001) in patients and controlled groups; respectively.

The differences between the results of this study and other investigators could be attributed to the differences in number of cases in various studies, association of other epidemiological factors affecting IL 8 and differences on the cut-off value of IL 8 normal value.

CONCLUSION

This study demonstrated that type 2 diabetes mellitus patients display a marked elevation of circulating IL-8 levels which identify subjects with worse inflammatory state and metabolic control. Prospective studies are needed to further evaluate the relevance of IL-8 in the disease process and to clarify whether it can be considered as a novel marker and a useful tool for risk stratification in T2D patients.

RECOMMENDATION

Further studies on IL-8 level in the serum of diabetic patients with and without diabetic complications. Further studies are required on large number of patients. To investigate serum IL-8 level before and after controlling the blood sugar levels as its level might be considered as an indicator for hyperglycemic control. Further studies could be valuable about cytokines inhibitors which might have a role in the prevention of diabetic progression and complications.

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