Original Article

The relationship between serum levels of il-12 and il-4 in patients with diabetes

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ABSTRACT

Introduction: diabetes is a prevalent disabling disease which is alarmingly increasing due to individuals' lifestyle; its level is 5% in Iran. This disease is diagnosed by FBS test. Objectives: the objective of this study was to investigate the FBS fluctuations with serum levels of IL-12 and IL-4 in patients with diabetes. Method: this study was conducted on the case and control groups. The case group included 45 patients with diabetes whose FBS level was higher than 125. 45 healthy people were also selected. The blood sample of all of them was taken and FBS test, IL-12, and IL-4 was done using nephelometry and ELISA method and in accordance with the manufacturer's kit instruction. Results: the average FBS level in the group with diabetes was approximately 175; it was 95 in the control group. Moreover, in the case group, it was higher than the normal level in 55.5% of the people with IL-4 and 58.7% of the people with IL-12. Conclusion: according to the data, the average serum levels of IL-4 and IL-12 in the people with diabetes whose FBS level was more than 125, was more than the healthy people. The statistical analysis of t-test was done and it was indicated that there is a statistically significant relationship between IL-12 level and FBS fluctuations in people with diabetes. However, there was not a statistically significant relationship between the increased FBS level and IL-4 level in people with diabetes.

Keywords: FBS, HbA1C, Interleukin 12, Interleukin 4

Introduction

Diabetes is one the prevalent non-communicable diseases which has many complications. In the early stages, half of the people are not aware of their disease since it does not have any symptom. As such, a series of factors are considered as risk factors for this disease and it is recommended to screen the individuals with these risk factors. Diabetes is a multifactor disease and it seems that it is caused by genetics, environmental, and immunologic factors [1].

Nowadays, due to the role of the cytokines and proteins of the acute phase, the relationship between them and different kinds of diseases is investigated.

Some research has been conducted to predict diabetes, indicating that low degrees of inflammation in the body may result in the clinical diabetes type 2 in long term. Moreover, there are different mechanisms showing that diabetes can be developed by cytokines. If the acute-phase proteins increase, inflammatory cells are more linked to adipose tissue and pancreatic beta cells, only affect pancreatic beta cells, help the apoptosis of beta cells, and cause diabetes type 2 [2]. There is a lot of evidence showing that both obesity and diabetes type 2 are associated with chronic inflammation. They are also associated with the increased level of acute-phase response protein of circulating blood and cytokines in people with diabetes [3].

Typical methods for diagnosing diabetes include biochemical tests of FBS and urine test. The physician may prescribe two tests for diagnosing hidden diabetes: FBS test and the test for glucose levels over the past 3 months (Hb A1C) [4].

Cytokines are a group of proteins secreted from different cells of the body such as the cells of the defensive system to respond to a stimulus, affecting the activities of the immune system. They are a group of proteins playing a major role in giving inflammatory responses to pathologic stimuli such as inflammation and tissue damage. Cytokine production is regulated by a domain of physiological stimuli such as physical exercise. The cytokines produced, expressed, and released from muscle fibers are known as myokines which are the impacts of paracrine, endocrine, and autocrine. Cytokines are responsible for transferring message between cells. The presence of cytokines results in a change in the behavior of the cells having secreted cytokine receptor such as cell growth, change, and death. The cytokine produced from a cell mostly

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acts and affects the cells around the same cell; yet, it may result in systematic action and effect on all organisms [5].

Inflammation is made when the immune cells of the body secret hormones named cytokines that is a normal reaction to the disease. However, when the cytokine hormones are secreted too much, this inflammation becomes uncontrollable and damages the body. These are the signs of interferon gamma [6].

The objective of the present study was to investigate the relationship between FBS fluctuations and serum levels of IL-12 and IL-4 in patients with diabetes type 2 in 2015 by referring to Ibn Sina Laboratory, Ilam Province. It is hoped that the results of this study can be used in the health planning of Iran.

Materials and Method

Cochran's formula

$$n = \frac{\frac{z^2 pq}{d^2}}{1 + \frac{1}{N}\left(\frac{z^2 pq}{d^2} - 1\right)}$$

was used to determine the sample size. The participants were selected by simple random sampling from different age groups (15 years old and above) who referred to Ibn Sina Laboratory, Ilam. This study is an analytical case-control research in which the individuals with an FBS level more than 125 mg/dl (45 people) were considered as the case group; the individuals with an FBS level lower than 125 mg/dl (45 people) were considered as the control group. The population of the study covers Ilam city. The inclusion criterion was having above 15 years old and the exclusion criteria were having pregnancy, cardiovascular diseases, asthma, and allergy.

The tests for determining the level of FBS, glucose levels over the past 3 months, and serum levels of IL-12 and IL-4 were done for all patients in the two groups according to the manufacturer's kit instruction. A t-test was used for data analysis based on the highness or lowness of the level of FBS, glucose levels over the past 3 months, and the values of the inflammatory cytokines in each group; ANOVA test was used to compare variables in different groups and assess the relationship between variables. Pearson correlation was used to assess the correlation between quantitative variables. The final report indicated that the host factors (FBS, HbA1C) are associated with cytokine secretion intensity.

Findings

The present study was developed and implemented so as to investigate the relationship between FBS and HbA1C fluctuations with serum levels of IL-12 and IL-4 in people with diabetes and healthy people. The FBS test and complementary tests were used to assess and diagnose the disease. 58 percent of the participants were female and the other ones were male. The average age of the patients was 50 years old and above. Generally, the average FBS was 175 and 8.8 A1C in the case group; the average level of IL-12 and IL-4 were respectively 34.2 and 35.7. Approximately, 58.7 percent of the individuals with high FBS had a higher level of IL-12 than the healthy people; there was a statistically significant difference ($P \leq 0.031$). Furthermore, 48.7 percent of the people with an FBS level more than the normal level had abnormal IL-4; there was not a statistically significant difference ($P \leq 0.094$).

Discussion

HbA1C shows glucose levels over the past 3 months. As such, the level of this factor is higher in the people with diabetes compared to the healthy people [4]. The investigations indicated that the average level of HbA1C in the case group and the control group was respectively 8.8 and 5.3; the average difference was 1.6. The HbA1C level is higher in the people with an FBS higher than the normal level compared to the healthy people.

Ikla et al. conducted a study and showed that the average difference of HbA1C in the two groups is 3.5 and the HbA1C level is higher in the people with diabetes compared to that in the control group [7]. Nayal et al. conducted a study and indicated that the average difference of FBS in the case and control groups is 80 and the average difference of HbA1C in the two groups is 3.5. They concluded that there is a statistically significant relationship between FBS and HbA1C and the people with diabetes have a higher level of HbA1C compared to the healthy people [8].

Dr. Soota et al. conducted a study on the relationship between FBS and HbA1C. They concluded that there is a significant relationship between FBS level and HbA1C and PPBS levels. They indicated that HbA1C is a golden standard in evaluating the glucose control, observance of diet, and the advancement and development of this disease in the past months [9].

IL-12 is a defensive cytokine secreted from defensive cells against autoimmune diseases [10]. In the present study, the average difference of IL-12 level in the case and control groups was 9.2. The IL-12 level in the case group was higher than the normal level compared to the control group.

Blaget et al. indicated that the average difference of IL-12 level in the case and control groups is 4.1 and the patients with diabetes have a higher level of IL-12 compared to the control group. The reason for the highness of IL-12 level in the patients with diabetes is not yet completely clear. However, Blaget et al. justified it due to autoimmune diabetes. Because diabetes is an autoimmune disease, the rate of cytokines secreted from the defensive system of the body increases [11]. Kridooki et al. conducted a study and showed that the average level of IL-12 had been increasing in the people recently afflicted with diabetes; however, it does not depend on the fluctuating level of HbA1C in the people with diabetes. Moreover, there has not been a statistically significant relationship between the level of IL-12 and HbA1C [12]. Teresa et al. conducted a study and concluded that there is a significant relationship between FBS and HbA1C. IL-12 is increasing in the people with diabetes,

makes the insulin resistant, and reduces its treatment [13]. Carolina et al. conducted a study on the relationship between IL-12, IL-18, and diabetes. The results showed that there is a relationship between the level of IL-12 and IL-18. However, the level of these cytokines was lower in the people with diabetes compared to the healthy people. They concluded that it may be effective to treat the people with diabetes through these cytokines [14]. In the present study, the average difference of the level of IL-4 was 1.4 in the case and control groups. There was not a large difference between two groups; however, the people with diabetes had a higher level of IL-4 compared to the healthy people.

Chernykh et al. conducted a study and indicated that the average difference of the level of IL-4 is 4 in the case and control groups. This value has a large difference with the average difference in the present study. The reason for this higher average difference may be due to the large population investigated in this study. They mentioned that the increased level of IL-4 in the people with diabetes is due to inflammation in the body and the development of pathogenesis processes of diabetes. They concluded that the patients with diabetes have a higher level of IL-4 than the healthy people [15].

Some studies were conducted on the relationship between several cytokines and diabetes. The results showed that there is a significant relationship between FBS and HbA1C in the people with diabetes; however, there was no significant relationship between the level of IL-4 and diabetes [16].

Conclusion

The present study aimed at investigating the relationship between the fluctuations of HbA1C and FBS and the level of IL-12 and IL-4. The results indicated that the increased rate of HbA1C and IL-12 has a direct relationship with the increased FBS in people. Where the fluctuations of glucose are higher, the immune responses also strongly move toward the increased level of IL-12. Moreover, it is a prognostic factor with regard to this disease; however, it did not have a direct relationship with the level of IL-4. One of the considerable findings of this study was the determination of the relationship between secretions of cytokines and glucose fluctuations

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