

## The relationship between type 2 diabetes mellitus and HbA1c and some immunological parameters

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### Abstract

This study knew that comparing type 2 diabetes mellitus and some pro-inflammatory immune factors, IL-6 and CRP clarified the higher glucose and their relationship in stimulating these immune factors. Type II diabetes mellitus, elevated incidence of disease, elevated IL6 and CRP II, in the absence of substrates run on elevated blood glucose.

### Introduction

Type 2 diabetes is one of the metabolic diseases that leads to high glucose in the blood, hyperglycemia due to the lack of pancreatic gland secretion of the hormone insulin, or the lack of response or resistance of body tissues to the action of this hormone (1). Statistics in the United States of America in 2015 indicated that approximately 30.3 million people, 9.4% of Americans, have diabetes (2). By 2030, it is expected that the number of people with diabetes around the world will increase by 439 million, or 7.7% of the world's population, and most of the increase will occur in developing countries by 69% compared to industrial countries, which account for 20% (3). Resistance to the effect of the insulin hormone is the main key to the events of diabetes and its future effects on the patient (4). The causes of the disease depend on a group of environmental factors, the most important of which are food, smoking and physical activity (5), And infection with various pathogens in addition to genetic factors, and these factors have important effects on stimulating the immune system responsible for the speed of the development of type 2 diabetes and its future effects on the patient (6,7). These causes work on changes inside the cells that lead to the secretion of pro-inflammatory factors in the blood circulation and a change in the infiltration of cells, so several immune cells enter the fatty tissue, pancreatic cells, and any tissue that participates in metabolism. ( 8,9,10),

These changes lead to inflammation, which has a role in developing insulin resistance and reducing the ability of pancreatic beta cells to produce the hormone insulin, thus causing type II diabetes (11,12). Several researchers have identified an increase in some inflammatory markers in the blood circulation of patients, such as interleukin-6 (IL-6) and C-reactive protein (CRP), which are essential in predicting the occurrence of type 2 diabetes or future related disorders (13,14, 15th). The International Expert Committee, represented by the American Diabetes Association (ADA), the European Council and the International Diabetes Federation, stressed the importance of adopting the measurement of HbA1c as a critical indicator in diagnosing type 2 diabetes (16, 17, 18). ). The current study aims to know the ability of patients to control glucose concentration and its importance in the occurrence of various disorders associated with type 2 diabetes, the possibility of using the index of intoxicating haemoglobin and immunological indicators in predicting type 2 diabetes,

especially among patients' relatives who do not have any clinical symptoms to get diabetes. The current study aims to evaluate the effect of high blood sugar on pathological factors. A comparison of the effect of diabetes mellitus between patients and healthy subjects.

### Material and Methods

Samples were taken during the period from 3/1/2021 to 6/12/2021, with 110 blood samples (5 ml) for each sample, according to the following distribution:

1- Patients group: Samples were taken from patients diagnosed with type 2 diabetes by specialized doctors at Al-Hakim Center for Diabetes and Endocrinology Research in Al-Sadr Medical Education City in Al-Najaf Al-Ashraf province, with 60 patients and an average age of 51.92 years (38-69 years).

2- Relatives group: the samples were taken from the relatives of patients without diabetes (apparently healthy) and not suffering from other chronic diseases. They numbered 30 individuals, with an average age of 36.73 years (22-50 years).

3- Control group: samples were taken from healthy people from any of the diseases, with an average age of 39.67 years (28-57 years), and their number is 30 individuals.

HbA1c (patients HbA1c  $\geq$  6.5%, relatives (onset of symptoms) 5.7% HbA1c  $\leq$  6.4%), control HbA1c  $\leq$  5.7%) (16, 17). The IL-6 concentration was measured using an enzyme-linked immunosorbent assay (ELISA). CRP was measured by the high-sensitivity LAX technology, an enhanced nephelometric assay of Menlatex. In contrast, HbA1c was measured using glycated haemoglobin's quantitative colourimetric method and colourimetric quantification of glycohemoglobin in whole blood.

### Statistical analysis:

The results of this study were analyzed according to the standard statistical methods using the statistical program known as the Statistical Package for Social Sciences SPSS (Seventeenth Edition) and using the one way of ANOVA test, were (mean  $\pm$  standard error) was measured to compare the average HbA1c ratio and the concentration of both IL6 and CRP among the different groups under study, under  $p < 0.05$ .

### Results:

We note from Table 1-1 that the average percentage of intoxicating haemoglobin HbA1c in the group of patients was 7.4840% with a significant difference ( $P \geq 0.05$ ) in comparison with the rest of the groups, as well as between the relative's group and the control group, where we notice a rise in this percentage in the relatives 6.0467% compared to the control group 5.1667 % and with a significant difference at the level of probability ( $P \geq 0.05$ ). In addition to the high concentration of IL6 CRP, 6.3134Pg/ml 2.3580mg/dl, with a significant difference ( $P \geq 0.05$ ) in the group of patients compared to the rest of the other groups, as well as the comparison between the two groups of relatives and the control, but without a significant difference (control Pg/ml 2.5500). And relatives 4.3190 Pg/ml), while there was a significant difference between the two groups for CRP (kins mg/dl 1.3110 and control mg/dl .66970).

**Table (1) comparison of Hba1c, IL6 and CRP between groups**

parameters	Group of patients mean $\pm$ SD)(	Group of relatives mean $\pm$ SD)(	Group of control )mean $\pm$ SD(
Hba1c %	.12975 ** $\pm$ 0 7.4840	.03643* $\pm$ 06.0467	.04557 $\pm$ 05.1667
IL6( Pg/ml)	.49161* $\pm$ 06.3134	.46255 $\pm$ 04.3190	.82829 $\pm$ 02.5500
CRP (mg/dl)	.20861** $\pm$ 02.3580	.16353* $\pm$ 01.3110	.09785 $\pm$ 0.66970

**\*\*It represents the significant difference for the group of patients with the level ( $P \geq 0.05$ ) and the rest of the groups**

**\*Represents the moral difference between the group of relatives and the control**

### Discussion:

The current study showed a high level of intoxicating haemoglobin (Hba1c) in the two patients and relatives compared to the control group. This result is consistent with Mohd (19). Also, the current study results agreed with the study of (20,21). The current study indicated a high concentration of (IL-6 CRP) in the two groups of patients and relatives compared to the control. The current study results agreed with the study of (19, 22), which confirmed the high C-reactive protein level in diabetic patients compared to the healthy group.

In contrast, the study (22) indicated an elevation of the C-reactive protein level produced in the liver depending on the stimulation of interleukin-6 and tumour necrosis factor-alpha. The study by (23) indicated that the increase in (IL-6 and CRP) together is essential evidence of resistance to the effect of the insulin hormone in the development of type 2 diabetes. In contrast, Pickup and his group indicated a high concentration of interleukin-6 in patients with type 2 diabetes in the study of Joachim and his group confirmed the importance of using interleukin-6 as an essential measure in predicting type 2 diabetes, both Konukoglu and his group and Cardellini and his group to the rise of interleukin-6 and tumour necrosis factor-alpha in patients, which was opposed by the result of the study Choi and his group, and the result of this study indicated the elevation of interleukin-6 in the pre-diabetes group compared to the control group. From all of the above, the current study confirms the possibility of using the previous criteria in detecting or predicting type 2 diabetes (24,25,26,27).

### References

- (1). American Diabetic Association (2010).Executive Summary: Standards of Medical Care in Diabetes—2010: Current criteria for the diagnosis of diabetes. Diabetes Care 33: S4-S10.
- (2). Centers for Disease Control and Prevention. National Diabetes Statistics Report (2017). Atlanta, GA: Centers for Disease Control and Prevention, U.S. Dept of Health and Human Services .2017.
- (3). Cinek O, Kramna L, Mazankova K, Odeh R, Allassaf A, Ibekwe MU, Ahmadov G, Elmahi BME, Mekki H, Lebl J, Abdullah MA. The bacteriome at the onset of type

- 1 diabetes(2018). A study from four geographically distant African and Asian countries. *Diabetes Res Clin Pract*; 144: 51-62.
- (4). Recasens M, Lopez-Bermejo A, Ricart W, et al. An inflammation score is better associated with basal than stimulated surrogate insulin resistance indexes. *Clin Endocrinol Metab* 2005; 90: 112–116.
- (5). Kolb H, Mandrup-Poulsen T. (2010)The global diabetes epidemic as a consequence of lifestyle-induced low-grade inflammation. *Diabetologia* ; 53: 10–20.
- (6). Howren MB, Lamkin DM, Suls J. (2009). A meta-analysis is associated with depression with C-reactive protein, IL-1, and IL-6. *Psychosom Med*; 71: 171–186.
- (7). Preshaw PM, Alba AL, Herrera D et al. (2012). Periodontitis and diabetes: a two-way relationship. *Diabetologia*; 55: 21–31.
- (8). Sattar N, Wannamethee SG, Forouhi NG. (2008).Novel biochemical risk factors for type 2 diabetes: pathogenic insights or prediction possibilities? *Diabetologia*; 51: 926–940.
- (9). Ouchi N, Parker JL, Lugus JJ, Walsh K. (2011). Adipokines in inflammation and metabolic disease. *Nat Rev Immunol*; 11: 85–89.
- (10). Osborn O, Olefsky JM. (2012). The cellular and signalling networks link the immune system and metabolism in disease. *NatMed*; 18: 363–374.
- (11). Donath MY, Shoelson SE. (2011). Type 2 diabetes is an inflammatory disease. *Nat Rev Immunol*; 11: 98–107.
- (12). Freeman DJ, Norrie J, Caslake MJ, et al. (2002). C-reactive protein is an independent predictor of risk for the development of diabetes in the West of Scotland Coronary Prevention Study. *Diabetes*; 51: 1596- 1600.
- (13). Fernandez-Real JM, Broch M, Vendrell J, et al. (2000). Interleukin-6 gene polymorphism and insulin sensitivity. *Diabetes*; 49: 517-520.
- (14). Greenfield JR, Campbell LV: (2006). Relationship between inflammation, insulin resistance and type 2 diabetes: ‘cause or effect’? *Curr Diabetes Rev*, 2:195-211.
- (15). The International Expert Committee. (2009). International Expert Committee report on the role of the A1C assay in diagnosing diabetes. *Diabetes Care*; 32 (7):1327-1334.
- (16). American Diabetic Association. (2010). Executive Summary: Standards of Medical Care in Diabetes—2010: Current criteria for the diagnosis of diabetes. *Diabetes Care*; 33: S4-S10.
- (17). Mark Livingston, Paul Masters (2013).Southern Derbyshire Shared Care Pathology Guideline: SDSCP-5 Version 1 Diagnosis of Diabetes Mellitus using HbA1c. Active Date 14.10.2011 Review Date October.
- (18). U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES National Institutes of Health: The A1C Test and Diabetes. NIH Publication No. 11–7816 September 2011.
- (19). Mohd. Idrees Khan, Kauser Usman, Fauzia Ashfaq, D. Himanshu, W. Ali, M.Z. Idris: Association of Hs-CRP and HbA1C with Microalbuminuria in Type-2 Diabetic patients in North India. *Biomedical Research* 2012; 23 (3): 380-384.



- (20). Nikzamir A, Esteghamati A, Feghhi M, Nakhjavani M, Rashidi A, Reza JZ. (2009). The insertion/deletion polymorphism of the angiotensin-converting enzyme gene is associated with albuminuria progression but not development in Iranian patients with type 2 diabetes. *J Renin Angiotensin Aldosterone Syst* ;10:109-14.
- (21). Azza M. El-Wakf, Tarek M. Abbas, Rizk A. El-Baz, Wafaa A. Mohammed. (2011). Role of hypertension and metabolic abnormalities in diabetic nephropathy among Egyptian patients with type 2 diabetes. *Nature and Science*; 9(7): 220-228.
- (22). Hansen D., P. Dendale, M. Beelen, R. A. Jonkers, A. Mullens, L. Corley et al., (2010). Plasma adipokine and inflammatory marker concentrations are altered in obese, unlike non-obese, type 2 diabetes patients. *Eur J Appl Physiol*. Jun; 109(3):397-404.
- (23). Frohlich M., A. Imhof, G. Berg G, (2000). Association between C-reactive protein and features of the metabolic syndrome: a population-based study. *Diabetes Care*.; 23:1835-1839.
- (24). Pickup JC, Mattock MB, Chesney GD, Burt D. (1997). NIDDM as a disease of the innate immune system: association of acute-phase reactants and interleukin-6 with metabolic syndrome X. *Diabetologia*;40:1286–92.
- (25). Joachim Spranger, Anja Kroke, Matthias Mohlig, Kurt Hoffmann, Bergmann Manuela M, Michael Ristow, et al. (2003). Inflammatory cytokines and the risk to develop type 2 diabetes. *Diabetes*;52:812–7.
- (26). Konukoglu D, Hatemi H, Bayer H, Bagriacik N. (2006). Relation between serum concentrations of interleukin-6 and tumour necrosis factor- $\alpha$  in female Turkish subjects with normal and impaired glucose tolerance. *Horm Metab Res*;38:34–7.
- (27). Cardellini M, Andreozzi F, Laratta E, Marini MA, Lauro R, Hribal ML, et al. (2007). Plasma IL-6 levels are increased in subjects with impaired glucose tolerance but not in those with impaired fasting glucose in a cohort of Italian Caucasians. *Diabetes Metab Res*;23(2):141–5.