

# Determination of IL-6 and CRP in Patients with Type Two - Diabetes Mellitus in Baghdad/ Iraq

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## Abstract

Diabetes mellitus (DM) type Two is a major worldwide health problem leading to an increase mortality and serious morbidity. Immunological disturbances involving the cell mediated immune system and improper-lymphocyte function contributes to the path physiological of type Two- DM. The study consist of 50 subjects, ages ranging between (15-85) years who attended to Al-Kazimaih medical hospital in Baghdad/Iraq which divided in to two groups; the first group consists 35 patient (20 females and 15 male) and the second 15 (5 female and 10 males) normal healthy as a control. The patients with type Two -DM were detected for IL-6 and CRP markers so as for control by ELISA test and agglutination test respectively. The results revealed that's no significant differences ( $p \geq 0.05$ ) between the level of CRP in patients type Two- DM and level of CRP in control. So as there were significant differences ( $p \leq 0.05$ ) between the levels of IL-6 concentrations in type Two- DM and control represented by increase of IL- 6 in control than in patients. This study aimed to assess and compare the level of serum IL-6 and CRP in patient of type Two- DM in Iraqi patients in Baghdad city.

**Key words:** IL- 6, CRP and diabetes mellitus type.

## Introduction

Diabetes mellitus is as an abnormal metabolic condition which caused by complications and inadequate insulin action. There are two types of diabetes, type one which known as insulin dependent diabetes mellitus (IDDM), and Type two which is non-insulin dependent diabetes mellitus (NIDDM) [1]. The characterization of pathogenesis of type Two- DM by a combination of insulin resistance at the level of muscles, fatty acids and failure of endocrine of pancreatic  $\beta$ -cells to equivalent for the increased insulin demand [2]-[3]. Type Two- DM was estimated to affect 15 million Americans and which was dramatically increasing in incidence [4]-[6]. The main physiological abnormalities are insulin resistance and impaired insulin secretion [7]-[9].

An accumulating body of evidence suggests that inflammation may be play a crucial intermediary role in pathogenesis, thereby linking diabetes with a number of commonly coexisting conditions thought to originate through inflammatory mechanisms [10].

Data studies, suggest that interleukin 6 (IL-6) and C-reactive protein (CRP), tow sensitive physiological markers of subclinical systemic inflammation, are associated with hyperglycemia, insulin resistance and overt type Two- DM [10]-[11]. Indeed,

recently studies postulated that type Two- DM, may represents a disease related the innate immune system (12) that a hypothesis of a particular interest because both of these inflammatory biomarkers (IL-6) and (CRP) which also are known to predict the development of cardiovascular disease in otherwise healthy populations [13]-[14].

Originally it was identified as IL-6 as a factor that induces the final maturation of B-cells into plasma cells. Also is involved in diverse biologic processes such as the activation of T cells, induction of the acute-phase response, stimulation of the growth and differentiation of hematopoietic precursor cells [15]. Another signs with more characters for inflammation in the body represented by (C) reactive protein (CRP) [16]. A detection tests for CRP are broadly corresponding and assessed for monitoring inflammation of cases and response for drug of inflammatory and immunological diseases such as rheumatoid arthritis. In addition, a CRP measurement has a practical test which a value tested when acute viral or bacterial infection is suspected [17]. The study was referred to investigate association of inflammation markers IL-6 and CRP in patients with type Two- DM and measurement of fasting glucose comparing with healthy control.

## **Material and Methods**

### **Sample collection**

The study content 50 patients afflicted with diabetic mellitus, their age ranging (15-85) years that attended from Al-kazimain Teaching Hospital in Baghdad/Iraq during the period of October 2015 until February 2016. The questionering of the patients involving patient's name, genus, type therapy, age and if accompanying disease were recorded. The patient's samples were compared with a total of 15 healthy (person volunteers) as a control with age of the patients group which were included in the present study. A venous blood samples were taken from the patients using a plastic disposable syringes (5ml) .The blood samples were centrifugation at (3000 rpm) for 15 min for sera separation which were stored in frozen at (-20C°) until assayed for markers detection represented by IL-6 and CRP(18) explained by:

### **Laboratory assessment**

The concentration of IL-6 was estimated in the separated sera by ELISA test as indicated by the procedure provided by the manufacturer (Koma Biotech Ink/Korea).The bio-source IL-6 is a solid phase are present in the specimens react with antibodies (MAb1) covered on the micro titer wells and with a antibody (MAb2) labeled with (HRP). While the determination of CRP in patients' sera samples by agglutination test according to (BioSystem, REF 31311). The statistically results for this study used an Excel 2010 program, by using Minitab software Version 6.

## **Result and Discussion**

Diabetes mellitus is a pancreatic endocrine disease defects on human body is a leading cause of mortality worldwide. It is characterized as a type Two- DM resulting from interaction of hereditary and environmental conditions that lead to a combination of insulin resistance complication in insulin related glucose defective secretion and insulin by pancreatic B-cell. The results of this study showed non-significant change in CRP in control and in group of patient's case with type Two - DM by probability of ( $p \leq 0.05$ ). The baseline characteristics of patients diagnosed with diabetes compared with control which were shown in table (1) represented by

genders of two groups of patients and control and median age which were 50 years in male and 39 years for female, whereas for control was 55 years for male and 62 years for females. The study denoted that 24 patients of type two - DM have CRP (+ve) and 11 samples CRP (-ve).

**Table (1): Explain the percentage of age and gender mean and CRP test.**

Groups	Gender (%)	median age	CRP-ve N(%)	CRP +VE N(%)	Total
Control	F 5(33.4)/M10(66.6)	M 50Y/F39 Y	2(13.3)	13(86.7)	15
Patient	F 20(57.2)/M15(42.8)	M 55Y /F 62 Y	11(31.4)	24(68.6)	35

There were no significant differences in blood sugar level in type two - DM ( $p \geq 0.05$ ) between CRP+ve and CRP-ve, while there was significant difference ( $p \leq 0.05$ ) among IL-6 level for CRP-ve and CRP+ve patient as shown in table (2).

**Table (2): Represent significant differences of blood sugar for IL-6 and CRP value for studied groups.**

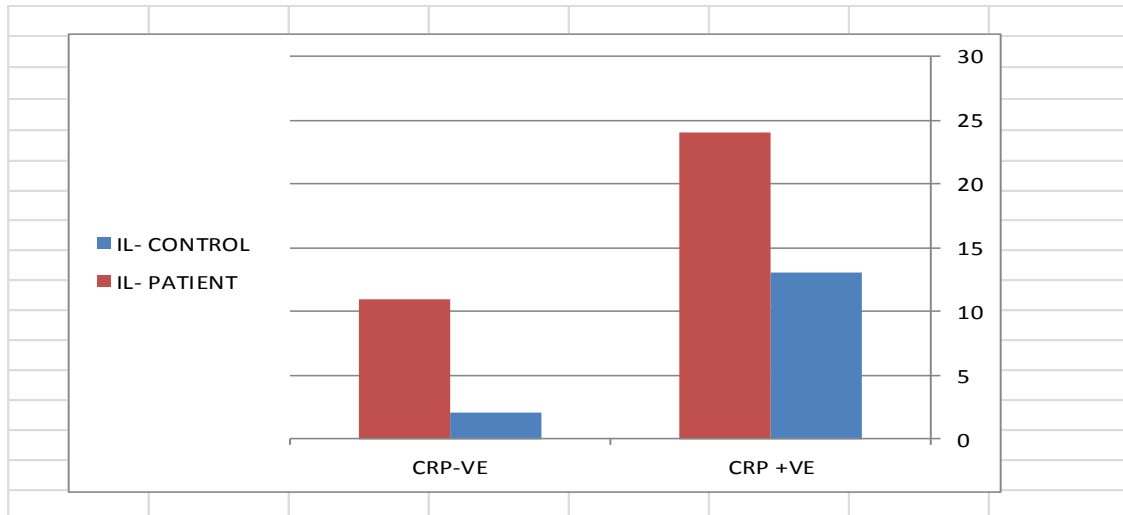
Test	CRP - (N 11)	CRP + (N 24)	F test	PV
	Mean $\pm$ SD	Mean $\pm$ SD		
B SUGAR	285.5 $\pm$ 68.8	282.6 $\pm$ 64.8	0.01	0.9 (NS)
IL-6 pg/ml	7.74 $\pm$ 4.22	8.14 $\pm$ 4.53	0.7	0.041 (S)

The study indicate IL-6 level not correlated to CRP (+ve) and CRP (-ve) ( $p \geq 0.05$ ) as show in table (3) and figure (1).

**Table (3): Correlation between IL-6 and blood sugar in CRP+VE and CRP -VE in diabetic patient**

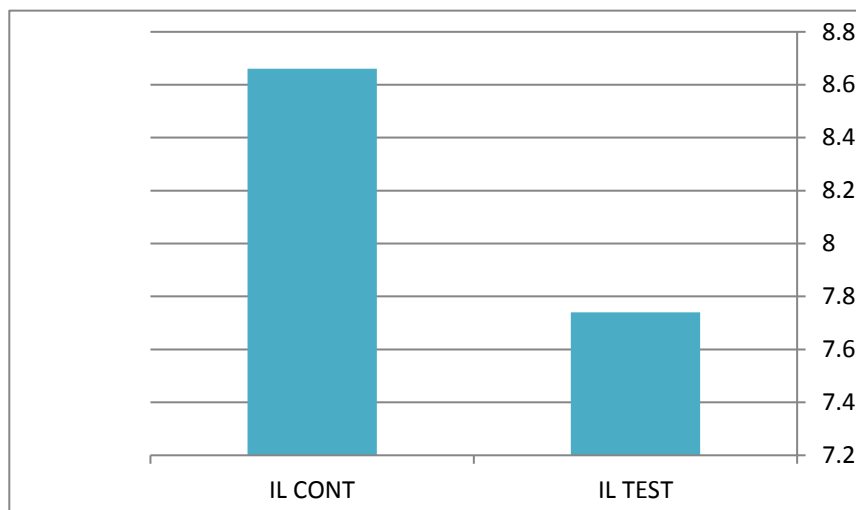
	Pearson correlation	P-Value	Result
CRP -VE (11)	0.191	0.573	NS*
CRP +VE (24)	0.14	0.557	NS

\*No- significant



**Figure (1):Correlation between IL-6 in blood sugar for CRP (+ve) and CRP(-ve) in type Two- DM patients.**

The comparison in IL-6 level between patient and control group was shown in figure -2 which indicate that patients of type Two - DM appeared low level of IL-6 than normal healthy control , the decrease in IL-6 level may be due to the depressed cell mediated immunity in the patients due to intake of medicines to control their blood sugar [18].



**Figure (2): Serum concentration of IL-6 pg/ml in type Two- DM patients and control.**

Finally, it's possibly that elevated CRP levels may largely reflect an innate system of macrophage so as adipocyte activation for instance, IL-6 and downstream CRP production may be associated with the core lease of other pathogenic substances arising from otherwise stimulated adipocytes [19]-[20] elevated CRP reflect the balanced altered and modification of cell mediated immunity in addition of adipocyte function, the ready availability of reliable and sensitive markers of this process may represent a novel approach for early identification .

## Conclusion

The result of present study suggest and support a possible role for inflammation and pathogenesis of type two- DM, in which elevated levels of C-reactive protein and interleukin-6.

## CONFLICT OF INTERESTS.

There are non-conflicts of interest

## References

- [1] N. A. Boon, N.R. Colledge and B.R. alker, J.A. Hunter, "Principles and practice Davidson's medicine". Churchill Livingstone, London.p:1126-1128, 2006.
- [2] S.V. Joshi, S.R. Tambwekar, H.L. Khadlia, K. Dha, "Role of Inflammatory Marker Interleukin 6 and Insulin in Diabetes and Diabetic Neuropathy", *Bombay Hospital*, vol. 50, no. 3, pp. 466, 2008.
- [3] P.Ole, M. and Thomas, "Interleukin 6 and diabetes, the good the bad or the indifferent", *Journal of Diabetes*, vol. 54, no. 2, pp. 114-124, 2005.
- [4] M. Harris, "Diabetes in America: Diabetes Data Compiled. Group NDD, ed. Bethesda, Md: National Institutes of Health, Dept of Health and Human Services 1-13. Publication (PHS) 95-1468. 1995.
- [5] M.I. Harris, K.M. Flegal, Cowie, C.C. et al., Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults: the Third National Health and Nutrition Examination Survey", *Journal of Diabetes Care*, 21:518-524, 1998.
- [6] J. Manson, "Risk modification in the diabetic patient. In: Manson J, Ridker P, Gaziano J, Hennekens C, eds. New York, NY: Oxford University Press, 241-273, 1996.
- [7] G.M. Reaven, "Banting lecture 1988: role of insulin resistance in human disease", *Journal of Diabetes*, vol. 37, pp. 1595-1607, 1988.
- [8] R.A. DeFronzo, "Lilly lecture 1987: the triumvirate: beta-cell, muscle, liver: a collusion responsible for NIDDM". *Journal of Diabetes*. pp. 37:667-687, 1988.
- [9] R.N. Bergman, "Lilly lecture 1989: toward physiological understanding of glucose tolerance: minimal-model approach", *Journal of Diabetes*, Vol. 38, pp. 1512-1527, 1989.
- [10] S. Sandler, K. Bendtzen, D.L. Eizirik, M. Welsh, "Interleukin-6 affects insulin secretion and glucose metabolism of rat pancreatic islets in vitro", *Journal of Endocrinology*, Vol. 126, pp. 1288-1294, 1990.
- [11] M. ]Frohlich, A. Imhof, G. Berg, et al., "Association between C-reactive protein and features of the metabolic syndrome: a population-based study", *Journal of Diabetes Care*, Vol. 23, pp. 1835-1839, 2000.
- [12] J.C. Pickup, and M.A. Crook, "Is type II diabetes mellitus a disease of the innate immune system?", *Journal of Diabetologia*, Pp. 41:1241-1248, 1998
- [13] P. M. Ridker, C.H. Hennekens, J.E. Buring, N. Rifai, "C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women", *New E.J. M.*, pp. vol. 342, 836-843, 2000.
- [14] P.M. Ridker, N. Rifai, M. J. Stampfer, C.H. Hennekens, "Plasma concentration of interleukin-6 and the risk of future myocardial infarction among apparently healthy men", *Journal of Circulation*, vol. pp. 101:1767-1772, 2000.

- [15] E.H. Choy and G.S. Panayi, "Cytokine pathways and joint inflammation in rheumatoid arthritis. *N. E. J. M.*, vol. 22, pp.13- 22, 2001.
- [16] C. Kluft, and M.P. deMaat, "Sensitive markers of inflammation make it possible to study the chronic process: the rise of interest in low levels of C-reactive protein", *Journal of Vascular Pharmacology*, 39(3) 99–104, 2002.
- [17] M. Cushman, A.M. Arnold, B.M. Psaty et al. "C-reactive protein and the 10-year incidence of coronary heart disease in older men and women", *Journal of the cardiovascular health study Circulation*, vol. pp. 112:25–31, 2005.
- [18] A. Najlla, A.A; Dhhan and H.A. AL-Dahhan, "Evaluation of ADA, IL-6 and TNF-alpha level in type 2 diabetes mellitus: with -and without hypoglycemic drugs", *Journal of Natural Sciences Research*, vol. 5, pp. 17, 2015.
- [19] G. Hotamisligil, P. Arner, J. Caro, R. Atkinson, B. Spiegelman, "Increased adipose tissue expression of tumor necrosis factor-alpha in human obesity and insulin resistance", *The Journal of Clinical Investigation*, vol. 95, PP. 2409-2415, 1995.
- [20] G. Hotamisligil, P. Peraldi, A. Budavari, R. Ellis, M. White, B. Spiegelman, "IRS-1-mediated inhibition of insulin receptor tyrosine kinase activity in TNF-alpha- and obesity-induced insulin resistance" *Journal of Science*, vol. 271, pp. 665-668, 1996.

## الخلاصة

يعد داء السكري (DM) Diabetes mellitus المعروف عالمياً كمشكلة صحية الذي يؤدي إلى الاعتلال و الموت . تتضمن الاضطرابات المناعية للمرض الاستجابة المناعية الخلوية للخلايا اللمفية T- cells التي تساهم في المسار الفسيولوجي Path physiological I لمرض السكري من النوع الثاني (Two- DM) Diabetes mellitus . شملت الدراسة (50) فرد تتراوح اعمارهم بين (15-85) سنة الذين حضروا الى مستشفى الكاظمية التعليمي في بغداد وقسمت الافراد الى مجموعتين الاولى تضمنت (35) مريض (20 انثى و 15 رجل) والمجموعة الثانية (15) فرد من الاصحاء كسيطرة . تم فحص انترلوكين - 6 و البروتين الفعال C- (CRP) لكل من مرضى السكري والاصحاء . فقد اشارت الدراسة بعدم وجود اختلاف معنوي ( $p \geq 0.05$ ) بين كل من CRP (+ve) و CRP (-ve-) في الدم السكري وكذلك بوجود اختلاف معنوي ( $p \geq 0.05$ ) في مستويات الانترلوكين - 6 IL 6 في المرضى السكري والاصحاء . لقد هدفت الدراسة تقييم ومقارنة انترلوكين -6 IL 6 و البروتين الفعال C- (CRP) في مرضى السكري في المرضى العراقيين في مدينة بغداد .

الكلمات الدالة: داء السكري، مستويات الانترلوكين، البروتين الفعال.