

## Study the relationship between CRP and some of cardiovascular complication factors in type 2 Diabetic

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### **ABSTRACT:**

Diabetes is associated with a pro-inflammatory condition and endothelial dysfunction. Various inflammatory markers such as C Reactive Protein CRP are significantly elevated in diabetic patients. Levels of these markers also correlate with the severity of diabetes and the presence of various complications. Therefore, we conducted this study to find high-sensitivity C-reactive protein (hsCRP) levels in type 2 diabetes mellitus and their relationship to other parameters such as the lipid profile for association with CVD. The study was included 112 samples were taken from patients with type2 (T2D) diabetes, which is inability of cells to receive glucose (insulin resistance) a, it was found that people who have only weak insulin secretion in the body, are most likely in the normal range for (HDL, LDL, TRI, CHOL). While for people with cells resistance, the results were higher than the normal (NR). This study examined the serum CRP concentration in relation to insulin resistance in type 2 diabetic patients. The statistical findings showed that serum CRP concentration in diabetic subjects significantly high.

In conclusion, Type II diabetes is a hemorheological disease in which hyperglycemia increases the shear stress contributing to inflammation and dysfunction of endothelium. The purpose of this study was to identify the relationship between serum C-reactive protein and glucose levels in noncontrolled type II diabetic subjects.

**Keywords:** high-sensitivity C-reactive protein(hsCrp), Triglycerides(Tri), high density lipid(HDL), Low density lipid (LDL), Cholesterol(CHOL), cardiovascular disease(CVD), Diabetes mellitus(DM).

دراسة العلاقة بين بروتين سي التفاعلي وبعض عوامل مضاعفات القلب

والأوعية الدموية لدى مرضى السكري من النوع الثاني

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### الملخص:

يرتبط مرض السكري بحالة مؤيدة للالتهابات و خلل وظيفي في بطانة الأوعية الدموية. علامات الالتهابات المختلفة مثل C Reactive Protein CRP مرتفعة بشكل ملحوظ في مرضى السكري. ترتبط مستويات هذه العلامات أيضًا بخطر مرض السكري ووجود مضاعفات مختلفة. لذلك أجرينا هذه الدراسة للعثور على مستويات البروتين التفاعلي عالي الحساسية (hsCRP) في داء السكري من النوع 2 و علاقتها بمعاملات أخرى مثل ملف الدهون المرتبط بأمراض القلب والأوعية الدموية. شملت الدراسة 112 عينة مأخوذة من مرضى السكري من النوع الثاني (T2D)، و هو عدم قدرة الخلايا على استقبال الجلوكوز (مقاومة الأنسولين) أ، و قد وجد أن الأشخاص الذين لديهم ضعف فقط في إفراز الأنسولين في الجسم، هم الأكثر عرضة للإصابة بمرض السكري. المعدل الطبيعي لـ (HDL، LDL، TRI، CHOL). بينما بالنسبة للأشخاص الذين لديهم مقاومة للخلايا، كانت النتائج أعلى من (NR). تناولت هذه الدراسة تركيز CRP في الدم وعلاقته بمقاومة الأنسولين لدى مرضى السكري من النوع الثاني. أظهرت النتائج الإحصائية أن تركيز CRP في الدم لدى مرضى السكري مرتفع بشكل ملحوظ.

في الختام، مرض السكري من النوع الثاني هو مرض نزفي حيث يزيد ارتفاع السكر في الدم من إجهاد القصد مما يساهم في التهاب و خلل في بطانة الأوعية الدموية. كان

الغرض من هذه الدراسة هو تحديد العلاقة بين بروتين سي التفاعلي ومستويات الجلوكوز التابع لمرضى السكري من النوع الثاني الغير منضبط.

الكلمات الدالة: بروتين سي التفاعلي عالي الحساسية (hsCrp)، الدهون الثلاثية (Tri)،  
الدهون عالية الكثافة (HDL)، الدهون منخفضة الكثافة (LDL)، الكوليسترول (CHOL)،  
أمراض القلب والأوعية الدموية (CVD)، داء السكري (DM).

## INTRODUCTION:

Diabetes mellitus (DM) is a group of metabolic diseases characterized by increase blood glucose level 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 various organs, especially the eyes, kidneys, nerves, heart, and blood vessels [1]. Type 2 diabetes characterized by hyperglycemia and dyslipidemia caused by islet  $\beta$ -cells being unable to secrete adequate insulin in response to varying degrees of long-standing insulin resistance [2].

The number of diabetic patients in the world has been estimated more than 175 million. DM is ranked 7th among leading causes of dead and has been related 3rd when all its fatal complications are taken in account. Patients with type-2 diabetes have increased risk of cardiovascular disease associated with atherogenic dyslipidemia. Coronary artery disease, especially myocardial infarction is the leading cause of morbidity and mortality worldwide [3].

C-reactive protein (CRP) is a sensitive marker for systemic inflammation. Recently, the relationship between inflammation and the development of Atherosclerosis disease, such as coronary heart disease (CHD)[4,5].

However, it is unclear whether elevated CRP levels only reflect a phenomenon accompanying atherosclerosis or whether CRP itself is involved in the initiation or progression of atherosclerosis [6].

Current evidence supports a central role of inflammation in the pathogenesis of atherosclerosis and diabetes. Type 2 diabetes is an inflammatory atherothrombotic condition associated with a high prevalence of cardiovascular disease. In patients with type 2 diabetes, low grade inflammation is reflected by increased plasma levels of several biomarkers of inflammation such as C-reactive protein (CRP). Small increases in CRP predict the likelihood of developing cardiovascular events both in diabetic and non-diabetic populations [7].

In addition, in apparently healthy subjects, increased levels of CRP predict the risk of developing type 2 diabetes. There is some evidence that CRP, besides its predictive role in determining cardiovascular risk, may represent an active participant in atherogenesis. CRP is expressed in human atherosclerotic plaques and vascular cells and monocytes / macrophages appear to represent a significant source of CRP in the inflammatory vessel wall. By activating the main cell types present in the atherosclerotic lesions, CRP generated within the coronary plaques may contribute to the development and progression of atherosclerosis.

Data on vascular CRP regulation are scarce. Current evidence suggests that inflammatory and metabolic factors associated with diabetes, such as high glucose, adipokines, modified lipoproteins and free fatty acids may trigger CRP production by endothelial cells, smooth muscle cells and monocytes / macrophages [7]. These data suggest that local CRP concentration in diabetic atherosclerotic plaques could be higher than in non-diabetic ones. Given the possible correlation between local CRP production and the degree of severity of coronary artery disease or the nature of the lesion, such alteration may contribute to the accelerated development of vascular disease in patients with type 2 diabetes. In Diabetic the liver is unable to store glucose in glycogen form which cause an accumulation in the blood and transformation into the form of triglycerides (smallest type of lipid), and this increases lipid in the blood (taking into account the difference in the value, depending

on the increase in the percentage and type of diabetes in the blood), occur due to chronic uncontrolled hyperglycemia in diabetic[8].

In the present study, we aimed to research association between serum lipid profile ( HDL, LDL, TRI, CHOL) and blood glucose, hypothesizing that early detection of lipid abnormalities can minimize the risk for atherogenic cardiovascular disorder and cerebrovascular accident in patients[9].

Glycated hemoglobin (HbA1c) is a routinely used marker for long-term glycemic control (5). In accordance with its function as an indicator for the mean blood glucose level, Hba1c predicts the risk for diabetic complication in diabetes patients.

Apart from classical risk factors like dyslipideia, elevated Hba1c has now been regarded as an independent 2 risk factor for CVD has shown to be increased by 18% for each 1% increase in absolute Hba1c value in diabetic population. Positive relationship between HbA1c and CVD has been demonstrated in nondiabetic cases even within normal range of Hba1c[10,11].

## **MATERIALS ANDMETHODS:**

### **Study population**

Blood samples were taken from 112 participants with type 2 diabetes mellitus. Samples were collected from individuals in the Ibn Al-Nafis Hospital for Diabetes and Endocrinology-Tripoli. Theirages ranged between 30-80 years. The study was carried out from December 2021 toFebruary2022.

Were excluded from the study Patients with severe liver dysfunction (viral hepatitis or cirrhosis), renal dysfunction (blood creatinine concentration > 1.5 mg/dL), known malignancy, or chronic inflammatory disease (e.g. arthritis, rheumatoid arthritis), and patients with a history of atherosclerotic disease.And most importantly, any patient infected with the Corona virus (COVIED 19) or feeling symptoms of the disease was excluded.

### Selection and collection of samples

7 ml of venous blood were drawn from each volunteer in this study, the blood was poured in 3 ml plane tube (clot activator), 2 ml glucose tube 3 (sodium fluoride) and were separated shortly after collection, 2 ml EDTA tube. Measurement of lipid tests (Cholesterol, Triglycerides, High-density lipoprotein (HDL), Low-density lipoprotein (LDL), C-reactive protein (CRP), Fasting blood glucose (FBS) and HbA1c were performed using an COBAS-INTEGRA 400 Plus device. The serum from all samples was transferred to the cuvette racks of COBAS INTEGRA 400 plus, manufactured in Germany [12].

### Statistical analysis

Collecting the sample, the statistical analysis will be carried out using the SPSS Program, version 22. Significant difference was considered at  $P < 0.05$ .

### RESULTS:

A total of 112 patients diagnosed as type 2 diabetes were selected to perform this study. The age was ranging between 30 to 80 years. It is noted that about (65/58.03%) of participants were women, while others (47/41.96%) were men (table 1).

The P-value of the C-reactive protein test was ( $P=0.117$ ), Cholesterol ( $P=0.024$ ), Triglycerides ( $P=0.001$ ), HDL ( $P=0.001$ ) and LDL ( $P=0.000$ ) (Table 2). Overall, 104 patients (92.8%) had at least one or more abnormal tests, 59 patients had elevated CRP, 23 patients had elevated cholesterol, 6 patients had elevated Triglycerides, 13 patients had elevated HDL, and 3 patients had LDL.

**Table 1. The number, sex and age of the samples**

Characteristics		Percent (%)
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	Number of patients (N)	
Sex		
Male	47	41.96
Female	65	58.03
Total	112	100
Age Group		
30-40	5	4.46
40-50	43	38.39
50-60	33	29.46
60-70	29	25.89
70-80	2	1.78
Total	112	100%

**Table 2. The results of lipid tests (Cholesterol, Triglycerides, High-density lipoprotein, Low-density lipoprotein, C-reactive protein**

Tests	Mean	Std. Deviation	T -Test	P -Value
Cholesterol	1.847	52.227	1.203	0.024
Triglyceride	6.76	3.375	-1.892	0.001
HDL	1.786	11.516	-1.591	0.001
LDL	1.201	44.576	1.06	0.000
CRP	108.53	53.160	-1.591	0.117

HDL= High-density lipoprotein& LDL = Low-density lipoprotein& CRP= C-reactiveprotein

## DISCUSSION:

Type II diabetes is an hem rheological disease in which hyperglycemia increases the shear stress contributing to inflammation and dysfunction of endothelium. The purpose of this study was to identify the relationship between serum C-reactive protein and glucose levels in noncontrolled type II diabetic subjects. A cross-sectional study was conducted, including 112 noncontrolled type II diabetic subjects that were assigned to two groups. were excluded from the study Patients with severe liver dysfunction (viral hepatitis or cirrhosis), renal dysfunction (blood creatinine concentration  $> 1.5$  mg/dL), known malignancy, or chronic inflammatory disease (e.g. arthritis, rheumatoid arthritis), and patients with a history of atherosclerotic disease. And most importantly, any patient infected with the Corona virus (COVIED 19) or feeling symptoms of the disease was excluded. One study on the effect of diabetes on the heart showed a doubling of heart risk. failure in diabetics compared to non-diabetics[13]. We also excluded subjects with hypertension due to left ventricular hypertrophy (IV) which has been clearly shown to be a strong, blood pressure-independent risk factor for cardiovascular disease and mortality, and in addition, hypertension was associated with an increased risk of CHF[14,15]. In our study we analyzed about 200 samples, in all, 104 patients (92.8%) had one or more abnormal tests, 59 patients had elevated CRP, 23 patients had elevated Chlo, and 6 patients had triplet elevation , and 13 patients had high HDL and 3 patients had high LDL, and this result was supported by a study conducted by many studies around the world showing the presence of heart and artery defects in individuals with type 2 diabetes[16]. An ubha Mahajan in Urban North Indians circulate lipid profile and C-reactive protein tests for 1,410 diabetic patients where 71.25% of the subjects had a In at least one lipid profile test, 46.8% was high Chlo/Tri and 48.5% had elevated levels of CRP[17]. Recently, Schalkwijk et al.[12] reported elevated hsCRP concentrations in patients with type 2 diabetes aged  $>30$  years. Kilpatrick et al.[18]. confirmed this observation and noted that six subjects with



coronary heart disease possessed significantly higher hsCRP concentrations than those without coronary heart disease. Only a few studies have evaluated the association between CRP concentration and development of carotid atherosclerosis in elderly subjects[18,19].A previous cross-sectional study described an association between CRP concentrations and severity of carotid atherosclerosis; however, the multivariate regression analysis failed to show a correlation between these two factors[18,19].Also, Folsom et al.[20] reported a weak association between hsCRP concentration and carotid IMT. In these studies, the subjects were elderly individuals who often had several risk factors including obesity, hyperlipidemia, and hypertension. In our study, however, the subjects were young and did not have any of these risk factors, with the exception of hyperglycemia. Therefore, the slight but significant increase in hsCRP concentration may affect the early stage of carotid atherosclerosis in these young subjects.

#### CONCLUSION:

In summary, the current study showed that T2DM patients with higher levels of CRP were susceptible to higher mindfulness, with a significant association in women but not in men. Further clinical studies would be warranted to confirm this observation.

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