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Research Article

The Correlation between Hemoglobin-A1C and C-Reactive Protein in Type-II Diabetic Patients

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Abstract

Background: Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia. It may be due to impaired insulin secretion or resistance to peripheral actions of insulin, or both. Poor glycemic control is significantly associated with the development of macro vascular complications. Earlier studies have indicated that C-reactive protein (CRP) is an important risk factor for cardiovascular disease as evident from its higher levels in people with diabetes mellitus compared to those without. Elevations in CRP are associated with an increased risk of insulin resistance by inhibiting skeletal muscle glucose delivery.

Objectives: The purpose of this study is to determine the relation between HbA1C and CRP in individuals with type 2 diabetes mellitus.

Methodolgy: A total of 140 patients were enrolled in the present study. They were divided into two groups according to if they are diabetic or non-diabetic as follows; 70 non-diabetics as the control group and 70 diabetics. Five milliliter of blood was withdrawn from venous blood by sterile syringes. The blood was collected in EDTA tubes to measure the HbA1c concentration and in clot tubes for biochemical assay (serum glucose and CRP concentrations).

Results: The result showed that the concentration of CRP and HbA1C among diabetic group was significant higher ($P<0.001$) when compared with non-diabetic group. In this study of 70 patients, the diabetic patients were divided into three groups according to the difference in HbA1C levels. Patients with HbA1C between of (5.0-7.0), HbA1C between of (8.0-10), and HbA1C of patients above 10. The results showed that there was a significant correlation between CRP and HbA1C ($P<0.05$) among the three groups.

Conclusion: In this study, a positive correlation between CRP and HbA1C was found. The finding regarding gender and age in this study suggested that CRP and HbA1C were not significantly associated with gender and age.

Key Words: type 2 diabetes mellitus, correlation, hemoglobin-a1c, hba1c, c-reactive protein, crp

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia. It may be due to impaired insulin secretion or resistance to peripheral actions of insulin, or both. According to the international diabetes federation (IDF), approximately 415 million adults between the ages of 20 to 79 years had diabetes mellitus in 2015 [1]. DM is proving to be a global public health burden as this number is expected to rise to another 200 million by 2040 [1, 2].

A new recommendation for the classification, diagnosis and screening of diabetes, announced at the American Diabetes Association (ADA) meeting in 1997, have changed the epidemiology of DM [3]. The new diagnostic criteria suggest that the diagnosis of DM be made on the basis of fasting plasma glucose only, in-contrast to the old criteria, which were based upon an oral glucose tolerance test (OGTT) [4]. It has been suggested that the OGTT should not be used for epidemiologic research, as it is an imprecise test with poor reproducibility [5].

Chronic hyperglycemia in synergy with the other metabolic aberrations in patients with diabetes mellitus can cause damage to various organ systems, leading to the development of disabling and life-threatening health complications, most prominent of which are microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular complications leading to a 2-fold to 4-fold increased risk of cardiovascular diseases. Persons older than 40 years of age should be screened annually. More frequent screening is recommended for individuals with additional risk factors for diabetes.[6]

Persistent hyperglycemia in uncontrolled diabetes mellitus can cause several complications, both acute and chronic. Diabetes mellitus is one of the leading causes of cardiovascular disease (CVD), blindness, kidney failure, and amputation of lower limbs. Acute complications include hypoglycemia, diabetic ketoacidosis, hyperglycemic hyperosmolar state, and hyperglycemic diabetic coma. Chronic microvascular complications are nephropathy, neuropathy, and retinopathy, whereas chronic macrovascular complications are coronary artery disease (CAD), peripheral artery disease (PAD), and cerebrovascular disease. It is estimated that every year 1.4 to 4.7% of middle-aged people with diabetes have a CVD event [7]. DM is broadly classified into three types by etiology and clinical presentation, type 1 diabetes, type 2 diabetes, and gestational diabetes (GDM). Some other less common types of diabetes include monogenic diabetes and secondary diabetes [8].

The concentration of HbA1c, generally expressed as the proportion of HbA that are HbA1c, is known to correlate with average blood glucose levels over the preceding 3 months [9]. Elevated glycohemoglobin (hemoglobin A1c [HbA1c]) is an established predictor for developing atherosclerosis beyond the risk associated with diagnosed diabetes (10). and is independently associated with cardiovascular disease and total mortality in nondiabetics (11). Insights gained from the link between inflammation and hyperglycemia can yield predictive and prognostic information for further risk [12].

CRP is a pentameric protein synthesized by the liver, whose level rises in response to inflammation. CRP is an acute-phase reactant protein that is primarily induced by the IL-6 action on the gene responsible for the transcription of CRP during the acute phase of an inflammatory/infectious process [13]. It has been studied as a screening device for inflammation, a marker for disease activity, and as a diagnostic adjunct [14]. In patients with type 2 diabetes, low-grade inflammation is reflected by increased plasma concentration of CRP. Low elevation in CRP level predicts the probability of developing cardiovascular events both in diabetic and non-diabetic populations. Inflammatory and metabolic factors associated with diabetes such as high glucose, adipokines, modified lipoproteins and free fatty acids may also trigger CRP production by endothelial cells, smooth-muscle cells and monocytes/macrophages. Thus, local CRP concentration in diabetic atherosclerotic plaques could be higher than in non-diabetic ones. So local CRP production may contribute to the accelerated development of vascular disease in patients with type 2 diabetes [15]. CRP may not only be implicated in the development of diabetes, but also in ongoing levels of hyperglycemia once diabetes is established [16]. Increased CRP levels predicted the new onset of diabetes even after adjustment for obesity, coronary risk factors and fasting insulin levels.

Analysis of data from NHANES III suggested that C-reactive protein (CRP), a principal downstream mediator of the acute phase inflammatory response, was significantly positively associated with HbA1c in a population of non-diabetic U.S. adults [17]. Elevated glycohemoglobin (hemoglobin A1c [HbA1c]) is an established predictor for developing atherosclerosis beyond the risk associated with diagnosed diabetes [10].

2. Objectives:

The aim of this study to investigating the relationship between HBA1c and CRP among patients with type 2 diabetes.

3. Materials and methods:

3.1. Subjects:

This study was performed in diabetic center in Zawia city-Libya. A total of 140 patients were enrolled in the present study. They were divided into two groups according to if they are diabetic or non-diabetic as follows; 70 non-diabetics as the control group and 70 diabetics.

Informed consent was taken from patient using questionnaire. Detailed history, physical examination which include gender, age, weight, the period of diabetic disease, the type of treatment, and if smoking or not were taken and write down. FBS, HbA1C, and CRP were measured

3.2. Sample collection:

Five milliliter of blood was withdrawn from venous blood sterile syringes, there capacity 5 ml for each subject. The blood was collected in EDTA tubes to measure the HbA1c concentration and in clot tubes for biochemical assay (FBS, and CRP concentrations). The blood samples were allowed to clot in the plain tubes for 20 minutes at room temperature.

3.3. Methods:

The serum was separated by centrifugation at 3000 rpm for 5 minutes, then each subject's serum was directly done by Mindray system BS200. HbA1c and biochemical assays were analyzed and determined by using Mindray Chemistry Analyzer (BS-200).

3.4. Statistical analysis:

Statistical analysis was done using SPSS package and Microsoft excel. Students T test, P values and Pearson correlation were used and calculated. P values < 0.05 was considered to be significant.

4. Results

In this study, the comparison of CRP and HbA1C concentration in diabetic and none-diabetic patients was done. The result showed that the concentration of CRP and HbA1C among diabetic group was significant higher ($P < 0.001$) when compared with non-diabetic group (Table 1).

Groups	n	Mean	Std. Deviation	Std. Error Mean	P-Value
HbA1C Control	70	5.26	0.42	0.50	0.001
HbA1C Diabetic	70	8.20	1.82	0.21	
CRP Control	70	2.19	1.18	0.14	0.001
CRP Diabetic	70	5.94	6.07	0.72	

Table 1: The comparison of CRP and HbA1C in non-diabetic and diabetic patients

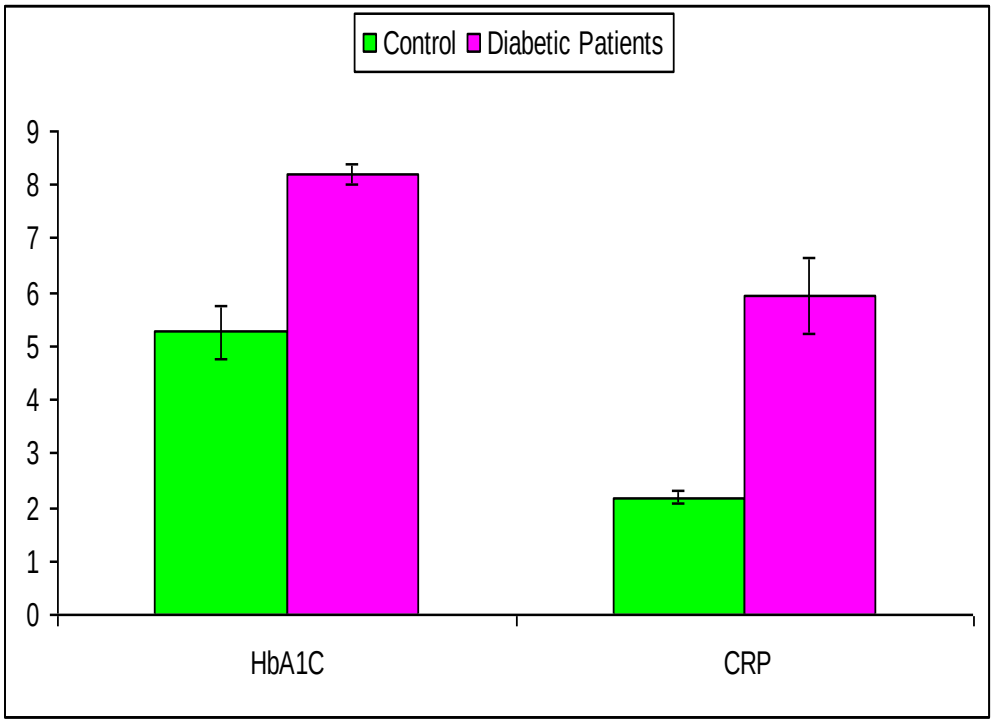

Figure 1: The comparison of CRP and HbA1C in control and diabetic patients

In this study of 70 patients, the mean HBA1C levels were 8.07 in males, while in female were 8.29. It was no significant difference between male and female (P>0.05), as shown in table 2 and figure. 2.

Also, in this study of 70 patients,23 patients were male and 47 were female with mean CRP levels of 5.39±0.99 and 6.17±1.22 respectively. There was no significant difference between male and female patients (p>0.05), as shown in table 2 and figure. 2.

Gender	n	Mean of HbA1C	Mean of CRP
Males	23	8.07	5.39
Females	47	8.29	6.17
Total	70	8.20	5.94

Table 2: HbA1C and CRP level in diabetic males and females.

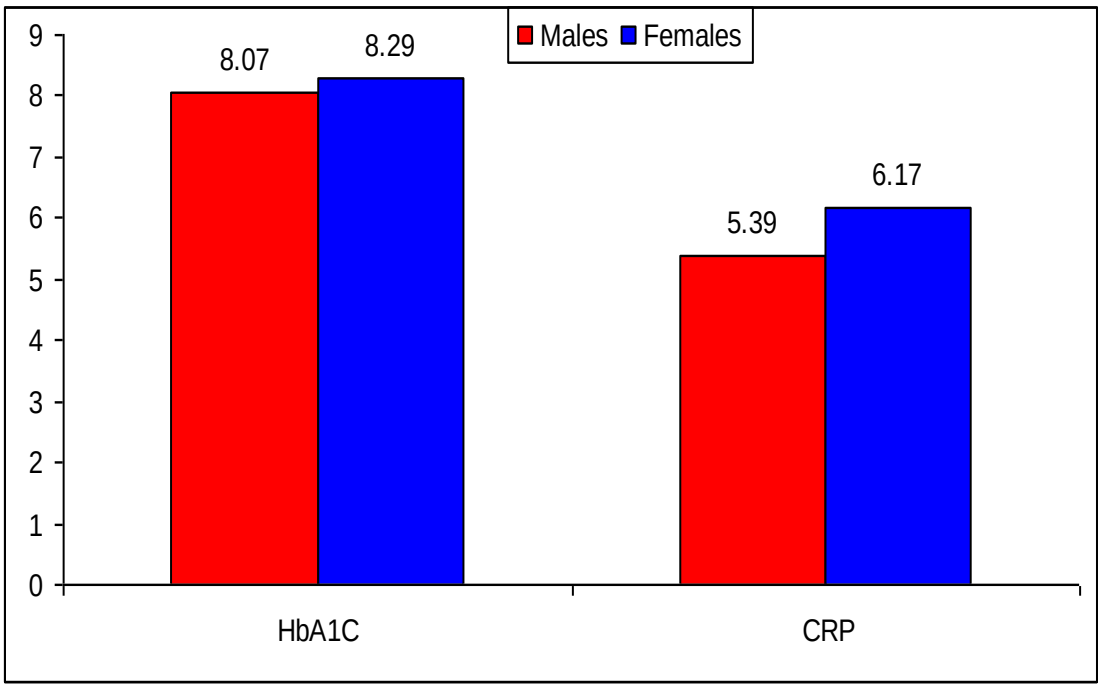

Figure 2: HbA1C and CRP level in diabetic males and females.

However, in this study of 70 patients, the diabetic patients were divided into three groups according to the different of HbA1C levels. Patients with HbA1C between of (5.0-7.0) were 34 patients, HbA1C between of (8.0-10) were 25 patients, while HbA1C of patients above 10 were 11 patients, and there mean CRP levels were 4.8±0.91, 4.4±0.66 and 9.31±2.94, respectively. The results showed that there was a significant correlation between CRP and HbA1C ($P<0.05$) among the three groups (Table 3 & Figure.3).

Parameters Groups		Number	Mean	Std. Deviation	Std. Error	F	*P- Value*
HbA1C groups	5.0 – 7.0	34	6.59	0.86	0.14	202.66	0.01
	8.0 – 10.0	25	9.07	0.74	0.15		
	> 10	11	12.02	0.55	0.17		
CRP groups	5.0 – 7.0	34	4.88	5.35	0.91	3.06	0.053
	8.0 – 10.0	25	4.43	3.32	0.66		
	> 10	11	9.31	9.31	2.94		

Table 3: The correlation between CRP and HbA1C in diabetic patients.

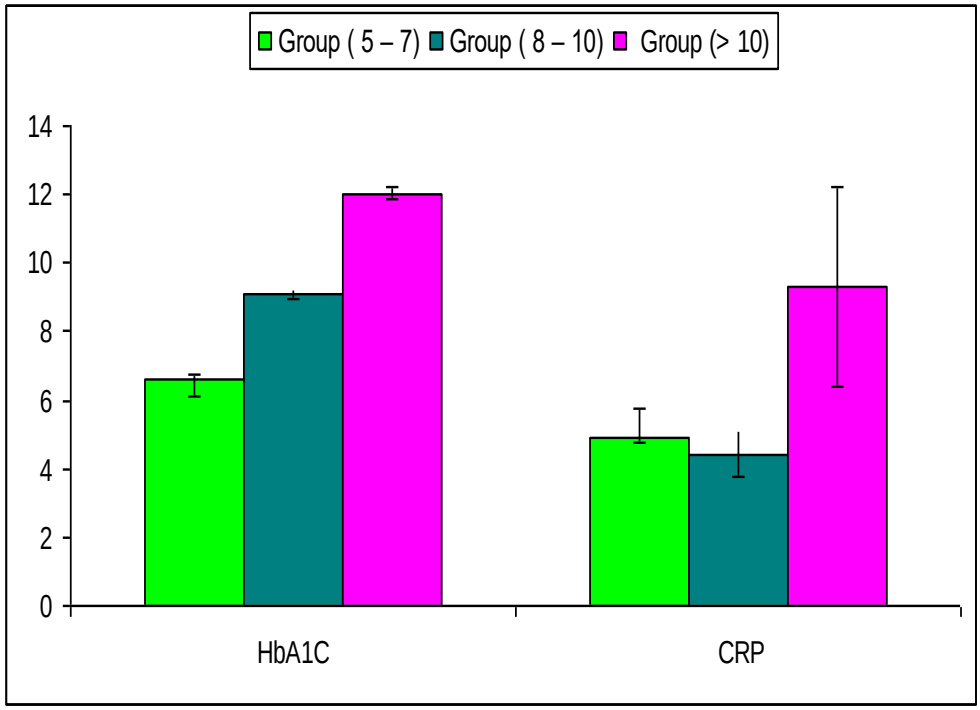

Figure 3: The correlation between CRP and HbA1C in diabetic patients.

As well as, in this study of 70 patients, HbA1C and CRP were correlated with age. So diabetic patents were divided into four groups according to the different of ages. The first group the age was between 30-39 years and the diabetic patents were 7 patients, with mean HbA1C and CRP of 8.23±1.97 and 6.29±2.11, respectively. Patients between ages 40-49 years were 16 with mean HbA1C and CRP of 8.08±1.99 and 4.89±1.46, respectively. Patients between ages 50-59 years were 16 with mean HbA1C and CRP of 8.51±2.14 and 4.88±0.69, respectively. While the patients above 60 years were 31 patients with mean HbA1C and CRP of 8.08±1.59 and 6.96±1.3, respectively. There was no significance between different age groups in this study (p>0.05) (Table 4 & Figure.4).

Parameters	Age Groups	Number	Mean	Std. Deviation	Std. Error	F	*P- Value*
HbA1C	30 – 39	7	8.23	1.97	0.75	2.08	0.11
	40 – 49	16	8.08	1.99	0.50		
	50 – 59	16	8.51	2.14	0.54		
	≥ 60	31	8.08	1.59	0.29		
CRP	30 – 39	7	6.29	5.59	2.11	0.71	0.55
	40 – 49	16	4.89	5.84	1.46		
	50 – 59	16	4.88	2.77	0.69		
	≥ 60	31	6.96	7.45	1.34		

Table 4: The levels of HbA1C and CRP of diabetic patients correlated with different age groups.

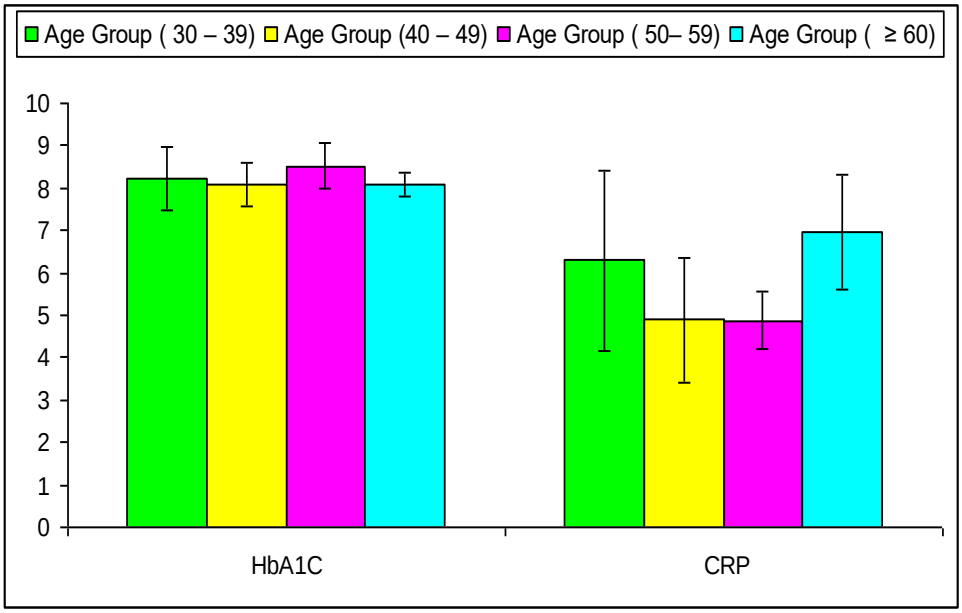

Figure 4: The levels of HbA1C and CRP of diabetic patients correlated with different age groups.

		CRP
HbA1C	Correlation coefficient (r)	0.250*
	P- Value	0.038

Table 5: The correlation between HbA1C and CRP in diabetic patients

5. Discussion

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia. It may be due to impaired insulin secretion or resistance to peripheral actions of insulin, or both. C-reactive protein (CRP). CRP is a pentameric protein synthesized by the liver, whose level rises in response to inflammation. Evidence of a relationship between HbA1c and inflammation was previously reported in studies that used CRP and WBC count to assess inflammation [18]. Analysis of data from NHANES III suggested that C-reactive protein (CRP), a principal downstream mediator of the acute phase inflammatory response, was significantly positively associated with HbA1c in a population of nondiabetic U.S. adults [17]. Therefore, this study has gone to the different factors that are related to both CRP and HbA1C of diabetic patients in zawia city. This study showed that a rise in HbA1C was significantly correlated with increasing values of CRP. It has showed that the concentration of CRP among diabetic group was higher ($p< 0.001$) when compared with non – diabetic group. Thus, the CRP levels affected the HBA1C levels. Our results were in agreement with previous study by king and others [19] which demonstrated that a higher HBA1C is significantly associated with a higher CRP level. Currently, the hypothesis explaining the relationship between markers of inflammatory response and insulin resistance is that chronic inflammation can act as an inducer of insulin resistance or stimulate CRP synthesis by an underlying disease, eventually leading to typer 2 diabetes. However, in this study of 70 patient, 23 of them were male and 47 were female. The results in this research showed that no difference in ($p>0.05$) levels of CRP and HBA1C between male and female. This result was in contrary to previous study by Hu et al. [19] which demonstrated that the association between CRP and risk of diabetes was stronger in women than man. The different between our result and the result of Hu et al. [19] could be due to a smaller number of samples that collected in this study.

6. Conclusion:

In this study of 70 diabetic patients, a positive correlation between CRP and HbA1C was found. The finding regarding gender and age in this study suggested that CRP and HbA1C were not significantly associated with gender and age.

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