

THE RELATIONSHIP OF C-REACTIVE PROTEIN WITH HbA1C LEVELS IN
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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) accounts for 90% of diabetes globally, characterized by elevated blood sugar due to genetic and environmental factors. It presents major health risks via organ complications. HbA1C serves as a crucial biomarker for long-term glucose management. Additionally, C-reactive protein (CRP) levels, linked to systemic inflammation, are affected by lifestyle choices and medications. **Aim:** To evaluate the correlation of serum CRP with glycated hemoglobin among Iraqi diabetic patients. **Patients and Methods:** A cross-sectional study was conducted at Al-Salam Teaching Hospital in Nineveh Governorate, Iraq, focusing on patients with type 2 diabetes mellitus diagnosed according to WHO criteria, from January to June 2025. Exclusions included individuals with established cardiovascular disease, chronic kidney disease, infections, hemolytic anemia, and those on statins or NSAIDs. Informed consent was obtained, and blood samples were collected to measure HbA1c and high-sensitivity CRP (hsCRP) levels, with HbA1c. **Results:** In this analysis of 60 patients with DM, data showed a mean HbA1c of 9.57 ± 1.911 and mean hsCRP of 6.42 ± 3.201 . Patients were categorized into three groups based on HbA1c levels, revealing a progressive increase in mean CRP levels corresponding to higher HbA1c levels. A Pearson correlation coefficient indicated a positive linear relationship between CRP and HbA1c, with a statistically significant p-value of 0.020. **Conclusion:** A significant correlation is observed between C-reactive protein levels and HbA1c levels in diabetic patients, with higher HbA1c values indicating poorer long-term glycemic control associated with elevated CRP levels.

KEYWORDS: C-Reactive Protein, Diabetic Mellitus, Glycated hemoglobin.**INTRODUCTION**

Type 2 diabetes mellitus (T2DM) is a multifactorial disease characterized by hyperglycaemia. The pathophysiology of impaired glucose homeostasis observed in T2DM is determined by the contribution of genetic, epigenetic and environmental factors, which collectively participate in the development of target tissue insensitivity to insulin, that is, insulin resistance.^[1] Diabetes is a major cause of disease and death, with the condition leading to a shortened life expectancy. The pathological state of diabetes consists of abnormalities in glucose, lipid and protein metabolism. Type 2 diabetes is the most frequently observed form of the disease accounting for 90% of diabetes cases worldwide.^[2]

The prevalence of diabetes mellitus is rising globally, making it a significant health concern worldwide. Diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia resulting from defects in insulin secretion, action, or both. Chronic hyperglycemia instigates long-term damage to the eyes, kidneys, nerves, heart, and blood vessels and is often associated with hypertension and dyslipidemia.^[3] The diabetes mellitus epidemic has prompted a critical need for prevention strategies and disease management plans to reduce morbidity and mortality.^[1] Diabetes affects several organs and systems, such as the kidneys, cardiovascular system, nervous system, gastrointestinal tract, liver, and eyes.^[2]

HbA1C is a key biomarker of average blood glucose levels over approximately three months and is widely adopted to evaluate glycemic status in diabetes management. Available data show that 70.1% of patients have HbA1C values below 7%, and there is a positive association between high-sensitivity C-reactive protein (hs-CRP) and HbA1C levels.^[4]

C-reactive protein (CRP) is a pentameric protein belonging to the pentraxin family, produced by the liver in response to inflammatory cytokines. Its synthesis can be stimulated by factors such as interleukin-1 (IL-1), tumor necrosis factor-alpha (TNF- α), and interleukin-6 (IL-6), all of which are produced and released by macrophages and adipocytes. CRP production begins between 4 and 6 hours following an inflammatory stimulus, with peak concentration reached within 36 to 50 hours. The physiological functions of CRP include activation of the classical complement pathway, stimulation of phagocytosis of various types of debris, and clearance of pathogenic substances.^[2] As a widely used marker of systemic inflammation, CRP binds autoantigens exposed during programmed cell death and

bacterial membranes and activates the complement system through the classical pathway, promoting phagocytosis. Elevated CRP levels are associated with chronic conditions including diabetes, atherosclerosis, and cancer, indicating the involvement of inflammatory mechanisms in these diseases.^[5] In diabetes, chronically elevated blood glucose leads to increased glycation of both cellular and extracellular proteins, glucose toxicity, and widespread organ damage. Concurrently, compromised antioxidant defense systems result in excessive free radical generation and oxidative stress.^[6]

The levels of C-reactive protein (CRP) and haemoglobin A1c (HbA1c) are influenced by various factors, such as lifestyle aspects, medication, and genetic factors, which should be considered when examining the link between these biomarkers. Lifestyle factors including physical inactivity, alcohol consumption, smoking, and obesity have been associated with elevated serum CRP concentrations. In type 2 diabetes mellitus patients, the use of antihypertensive drugs and oral antidiabetic drugs has been positively correlated with serum CRP concentrations.^[1] Conversely, the use of 0.

Table 1: Descriptive Statistics for HbA1c and hsCRP.

variables	N	Minimum	Maximum	Mean	Std. Deviation
HbA1c	60	5.22	13.08	9.5777	1.91137
hsCRP	60	1.15	10.00	6.4242	3.20126

The patients are divided into three groups based on their HbA1c levels, following standard clinical guidelines and the table (2) clearly showed a progressive increase in

mean CRP levels as the mean HbA1c increases across the groups.

Table 2: Glycemic Control Groups and the mean hsCRP.

Glycemic Control Group	HbA1c Range (%)	N	HbA1c Mean $\pm$ SD (%)	CRP Mean $\pm$ SD (mg/L)
Good Control	< 7%	3	6.50 $\pm$ 0.31	1.55 $\pm$ 0.54
Fair Control	7%–9%	9	8.10 $\pm$ 0.55	4.19 $\pm$ 0.94
Poor Control	> 9%	28	10.05 $\pm$ 0.69	8.29 $\pm$ 1.01

Table (3) demonstrated the correlation of CRP with HbA1c and provided the Pearson correlation coefficient (r) for all 60 patients, which measures the strength and direction of the linear relationship between CRP and HbA1c. this table indicated a positive linear relationship

between CRP and HbA1c. As HbA1c levels rise, CRP levels consistently increase and the p-value of 0.020 signified that this correlation is statistically significant and not due to random chance.

Table 3: Correlation between HbA1c and hsCRP.

		hsCRP	HbA1c
hsCRP	Pearson Correlation	1	0.299*
	Sig. (2-tailed)	-----	0.020
	N	60	60
HbA1c	Pearson Correlation	0.299*	1
	Sig. (2-tailed)	0.020	-----
	N	60	60
*Correlation is significant at the 0.05 level (2-tailed).			

By referring the linear regression, the table (4) revealed a significant statistical regression of hsCRP with HbA1c

under the equation of Predicted (hsCRP)=1.631+0.5(HbA1C)+error.

Table 4: Linear regression of hsCRP with HbA1c.

Model	Unstandardized Coefficients		Standardized Coefficients	t	p-value
	B	Std. Error	Beta		
(Constant)	1.631	2.049	-----	0.796	0.429
HbA1c	0.500	0.210	0.299	2.384	0.020

a. Dependent Variable: hsCRP

DISCUSSION

The findings of this study highlight a strong association between CRP and HbA1C, reinforcing the concept that HbA1C levels and inflammation are closely linked. The adverse impact of elevated HbA1C on inflammatory status measured by CRP suggests that enhancing glycemic control before persistent increases in HbA1C and inflammatory markers could be crucial in managing diabetic patients at heightened risk of cardiovascular disease.^[1] Future investigation may focus on the progression to more advanced diabetic stages and explore whether anti-inflammatory therapies could complement antidiabetic drugs, thereby improving overall patient outcomes.^[2]

The current study showed that the correlation coefficient of hs-CRP with the HbA1C was 0.299 and showed a significant statistical association. This findings was corresponding to that reported by Seo and Park study.^[7] Many studies have investigated the possible relationship between CRP and HbA1C levels. Petchiappan et al.^[8] conducted found positive correlation was observed between HbA1c and CRP at baseline ($r=0.32$, $p=0.10$). Additionally, Nagalakshmi study^[9] provided comprehensive evidence supporting the role of C-reactive protein (CRP) as an inflammatory biomarker linked to poor glycemic control and early diabetic complications. The significantly elevated CRP levels in type 2 diabetic patients compared to non-diabetic controls (5.05 ± 1.87 mg/L vs. 2.13 ± 0.76 mg/L; $p < 0.001$). The Sasidharan et al.^[10] and Habib et al.^[11], study demonstrated higher CRP in diabetic cohorts and correlated it with worsening metabolic parameters and insulin resistance.

In our study, the strength of association between CRP and glycemic control was notable run in parallel to the findings reported by Tang et al.^[12] and Elimam et al.,^[13]. A robust positive correlation was observed between CRP and HbA1c indicated that systemic inflammation escalates with deteriorating glycemic regulation and this might be related to chronic hyperglycemia which induced oxidative stress, endothelial dysfunction, and systemic inflammatory cascades. Thair et al.,^[14] concluded that well glycemic control is foremost to the decline in HbA1c moreover caused a reduction in CRP levels when HbA1c was ≤ 7 .

Among the several biomarkers that have been proposed for CV risk stratification, hs-CRP appears to donate to the identified people at risk of developing CVD, this was clearly stated in the study conducted by Fonseca and Izar.^[15] Data from Abdelnabi and Sadek study,^[16]

confirmed that the high levels of hs-CRP and OR= 1.157 are associated with diabetes by high concentration in diabetic patients paralleled to the lowest concentration in the controls.

CONCLUSION

A clear and significant correlation exists between C-reactive protein (CRP) levels and HbA1c levels in diabetic patients. Higher HbA1c values, which indicate poorer long-term glycemic control, are consistently associated with elevated levels of CRP, a marker of systemic inflammation. This relationship suggests that poorly managed diabetes is not merely a metabolic dysfunction but is also driven by or contributes to chronic, low-grade inflammation.

CONFLICTS OF INTEREST

The author declare that they have no conflicts of interest.

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