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Research Article

Relation of CRP Level with the Severity of Coronary Artery Stenosis in Diabetic Patients

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Abstract

Background: Atherosclerosis is a disease characterized by the deposition of lipids on the inner walls of blood vessels. Diabetes is a significant risk factor for atherosclerosis. C-reactive protein (CRP) is a marker of systemic inflammation and an independent risk factor for cardiovascular disease (CVD). This study aimed to investigate the relationship between serum CRP levels and the severity of coronary artery disease in diabetic patients.

Materials and methods: This cross-sectional analytical study was conducted on 185 diabetic patients referred for coronary angiography based on non-invasive test indications. A checklist was used to collect demographic data, blood pressure readings, and duration of diabetes was completed, and CRP testing was performed for each patient. Coronary angiographic data were also collected, including the type and severity of involved vessels reported by two cardiologists.

Results: There was a statistically significant relationship between serum CRP level and severity of coronary artery disease ($p = 0.009$). Additionally, there was a significant relationship between the duration of diabetes and the severity of coronary artery disease (p – value = 0.006).

Conclusion: We found a significant relationship between serum CRP levels and the severity of coronary artery stenosis and between the duration of diabetes and the severity of coronary artery stenosis.

More Information

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Keywords: CRP; Coronary artery disease; Diabetes mellitus

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Introduction

CVD is the primary cause of death worldwide. The morbidity and mortality rates among patients with CAD are significantly elevated when diabetes is present, contributing to approximately half of the deaths. Thus, identifying CAD and its risk factors is imperative for enhancing treatment and prevention strategies, particularly in diabetic patients [1]. Over 200 risk factors and social and personal behaviors can influence CAD [2-4]. Inflammation plays a crucial role in CAD's development, advancement, and prognosis, and is extensively recognized as an independent risk factor for CAD onset. It participates in numerous stages of atherosclerosis, and initiating inflammatory reactions could significantly contribute to plaque instability.

CRP, produced by the liver, serves as a valuable marker for detecting and assessing infection, tissue damage, inflammatory conditions, and associated diseases. Elevated levels of high-sensitivity CRP (hs-CRP) have been linked to unfavorable events in a range of cardiovascular conditions, such as heart failure, ischemic stroke, atrial fibrillation, and type 2 diabetes mellitus (T2DM) [5]. CRP has been demonstrated to independently correlate with an increased occurrence of future cardiovascular events in multiple prospective cohort studies, encompassing both at-risk populations and those with CAD [6]. In this study, we investigate the relationship between hsCRP levels and the severity of CAD in diabetic patients.

Material and methods

This analytical cross-sectional study was conducted on diabetic patients with indications for coronary angiography based on non-invasive tests who were admitted to the angiography department of Shahid Sadoughi Hospital in Yazd from 2013 to 2016. In this study, simple random sampling was used. The researcher completed data collection by observing the angiography results and a CRP test for each patient. The CRP testing was performed using one cc of venous blood with the CRP-LATEX kit from the Bionik company. The CRP level was

categorized as < 6 mg/L and ≥ 6 mg/L, and their classification and relationship with the severity of coronary artery stenosis were judged statistically. This study was approved by the ethics committee (IR.IAU.KHUISF.REC.1400.141).

Data analysis

The data was analyzed using SPSS 17 statistical software on the computer. Analysis of variance, t-test, and Spearman's correlation coefficient test were used to analyze the data. *p* - value ≤ 0.05 was considered significant.

Results

In this study, the relationship between serum level of CRP and severity of coronary artery stenosis in diabetic individuals was investigated. For this purpose, 185 diabetic patients who were candidates for angiography were selected. 92 (49.7%) were male and 93 (50.3%) were female. The mean age of the study sample was 61.96 ± 11.2 years, ranging from 36 to 89 years. The mean duration of diabetes in these patients was 5.05 ± 2.4 years, ranging from 6 months to 20 years. In 94 individuals, diabetes duration was ≤ 4 years; in 91, it was more than 4 years. In this research, systolic and diastolic blood pressure were measured, with diastolic blood pressure ranging from 60 to 100 mmHg.

In the frequency distribution of vessel involvement in the examined samples, the highest frequency belongs to 2VD, with 46 individuals (24.86%), and the lowest frequency is related to LM (left main) artery stenosis, with five individuals (2.7%) (Tables 1,2).

The mean duration of diabetes was 5.05 ± 4.23 years (95% CI: 4.44 - 5.67). This number was 7.04 in 3VD patients, the highest; in LM and No CAD patients, it was 3.60, the lowest. These differences were significant based on the variance test analysis and *p* - value = 0.006. According to our data, there is a direct relationship between the severity of coronary artery stenosis and the duration of diabetes (Table 3).

The average diastolic blood pressure in patients with a confidence limit of 95% (7.65 to 7.89) was 7.77 ± 0.82. This number was 7.93 in regular patients, the highest, and 7.65 in mild CAD, the lowest. These differences were tested by analysis of variance and were not significant, with a *p* - value of 0.73. According to this study, there is no significant relationship between the severity of coronary artery occlusion and diastolic blood pressure (Table 4).

The duration of diabetes is divided into two groups, under three years and over 3 years, and in the whole group under three years, the average serum CRP was 6.09 ± 5.09. This number was the highest in 3VD-LM patients and the lowest in mild CAD. These differences were tested using ANOVA and were found to be statistically significant (*p* - value=0.002). There was a substantial relationship between the severity of coronary artery disease and the serum CRP level in individuals with a diabetes duration of less than three years. Still, no significant relationship was found in the group with a history of diabetes of more than four years (*p* - value = 0.432) (Table 5).

In this Table, the blood pressure of the patients was divided

Table 1: Distribution of Vessel Involvement in Coronary Angiography.

Angiography results	No CAD	Mild CAD	1VD	2VD	3VD	LM
Frequency (Percent)	29 (15.67)	23 (12.43)	38 (20.5)	46 (24.86)	44 (23.78)	5 (2.7)

Table 2: Average serum CRP level and the severity of coronary artery stenosis.

Vascular occlusion severity	Number of samples (percent)	mean CRP (mg/l)	SD	95% CI Confidence intervals	
				upper limit	lower limit
No CAD	29 (15.67)	6.93	5.90	9.17	4.68
Mild CAD	23 (12.43)	4.86	2.88	11.6	62.3
1VD	38 (20.5)	5.50	3.05	6.50	4.49
2VD	46 (24.86)	6.45	4.72	7.86	5.05
3VD	44 (23.78)	8.34	5.80	10.10	6.57
LM	5 (2.7)	11.80	9.78	23.94	0.34

Table 3: The average duration of diabetes and severity of coronary artery stenosis.

Vascular occlusion severity	Number of samples (percent)	The average duration of diabetes (year)	SD	95(CI)% Confidence intervals	
				lower limit	upper limit
No CAD	29 (15.67)	3.60	3.48	2.27	4.92
Mild CAD	23 (12.43)	4.80	4.26	2.96	6.64
1VD	38 (20.5)	4.07	3.05	3.07	5.08
2VD	46 (24.86)	5.17	4.46	3.84	6.50
3VD	44 (23.78)	7.04	4.87	5.56	8.52
LM	5 (2.7)	3.60	1.34	1.93	5.26
Total	185 (100%)	5.05	4.23	4.44	5.67

Table 4: The mean diastolic blood pressure and severity of coronary artery stenosis.

Vascular occlusion severity	Number of samples (percent)	Mean diastolic blood pressure	SD	95(CI)% Confidence intervals	
				lower limit	upper limit
No CAD	29 (15.67)	7.93	0.59	7.70	8.15
Mild CAD	23 (12.43)	7.65	1.19	7.13	8.16
1VD	38 (20.5)	7.73	0.64	7.52	7.94
2VD	46 (24.86)	7.84	0.74	7.64	8.09
3VD	44 (23.78)	7.68	0.95	7.39	7.97
LM	5 (2.7)	7.80	0.44	7.24	8.35
Total	185 (100%)	7.77	0.82	7.65	7.89

Table 5: The mean serum CRP level in the studied samples according to the severity of coronary stenosis and duration of diabetes.

Duration of diabetes (year)	Severity of coronary stenosis	Number of samples	Mean CRP(mg.1)	SD	*p* - value
0.5-3	No CAD	21	6.33	6.13	0.002
	Mild CAD	13	4.61	3.42	
	1VD-2VD	45	4.97	2.37	
	3VD-LM	15	10.40	8.04	
	Total	94	6.09	5.09	
4-20	No CAD	8	8.50	5.29	0.432
	Mild CAD	10	5.20	2.09	
	1VD-2VD	39	7.23	5.16	
	3VD-LM	34	7.94	5.26	
	Total	91	7.38	4.98	

into two ranges, normal and high blood pressure, according to the measurement of the blood pressure of the patients, and the range of the normal blood pressure below 135 mm Hg for systolic and 85 mm Hg for diastolic blood pressure was considered. The variance test analysis was performed. A significant relationship was not found between the severity of coronary artery Stenosis and serum CRP level in the normal blood pressure group (p - value=0.065) and the high blood pressure group (p - value = 0.153) (Table 6).

This study examined both men and women. The average serum CRP in men was 6.98 ± 5.49 and 6.47 ± 4.61 in women. These differences were tested by analysis of variance, and no significant relationship between the severity of coronary artery stenosis and serum CRP level in men (p - value = 0.114) and women (p - value = 0.108) was found (Table 7).

This study divided patients into ages 38 to 59, 60 to 69, and 70 to 89. Additionally, the severity of coronary artery stenosis was categorized into four groups: without CAD, mild coronary artery stenosis, one vessel stenosis (1VD), two vessel stenosis, and severe stenosis of three vessels and LM. These differences were statistically tested using analysis of variance. In the 38- to 59-year-old age group, a p - value of 0.350 indicated no significant relationship between the severity of coronary artery stenosis and serum CRP levels. In the 60- to 69-year-old age group, a p - value = 0.530 suggested no significant relation between the severity of coronary artery stenosis and serum CRP levels. However, in the 70- to 89-year-old age group, a substantial p - value of 0.034 indicated a meaningful relationship between the severity of coronary artery stenosis and serum CRP levels (Table 8).

Table 6: The mean serum CRP level and the severity of coronary artery disease.

	Severity of coronary stenosis	Number of samples	Mean CRP (mg.L)	SD	p - value
NL	No CAD	21	6.42	5.87	0.065
	Mild CAD	17	5.00	3.35	
	1VD-2VD	64	5.93	4.13	
	3VD-LM	36	8.33	5.93	
	Total	138	6.51	4.94	
HTN	No CAD	8	8.52	6.18	0.153
	Mild CAD	6	4.50	0.54	
	1VD-2VD	20	6.30	3.90	
	3VD-LM	13	9.76	7.24	
	Total	47	7.36	5.40	

Table 7: The mean serum CRP level in the studied samples according to coronary artery disease severity and sex.

Sex	Severity of coronary stenosis	Number of samples	Mean CRP (mg.1)	(SD)	p - value
Male	No CAD	11	7.54	7.64	0.114
	Mild CAD	6	4.66	3.44	
	1VD-2VD	46	6.00	3.37	
	3VD-LM	29	8.82	7.10	
	Total	92	6.98	5.49	
Female	No CAD	18	6.55	4.75	0.108
	Mild CAD	17	4.94	2.77	
	1VD-2VD	38	6.05	4.80	
	3VD-LM	20	8.50	4.96	
	Total	93	6.47	4.61	

Table 8: Mean CRP level in the studied samples according to coronary artery disease severity and age.

Age	Severity of coronary stenosis	Number of samples	Mean CRP (mg.1)	(SD)	p - value
38-59	No CAD	19	5.00	4.50	0.35
	Mild CAD	14	5.07	3.70	
	1VD-2VD	48	4.97	2.40	
	3VD-LM	16	6.81	5.24	
	Total	97	5.29	3.64	
60-69	No CAD	6	8.00	6.22	0.53
	Mild CAD	7	4.57	0.53	
	1VD-2VD	18	7.66	6.06	
	3VD-LM	18	8.50	6.84	
	Total	49	7.57	5.94	
70-89	No CAD	4	14.50	6.02	0.03
	Mild CAD	2	4.50	0.70	
	1VD-2VD	18	7.16	4.51	
	3VD-LM	15	10.93	6.22	
	Total	39	9.23	5.79	

Discussion

Inflammation and lipid signaling are involved in the pathogenesis and progression of coronary artery disease and diabetes. In this research, we aimed to evaluate the relationship between serum CRP level and the severity of coronary artery disease and the relationship between the duration of diabetes and the severity of coronary artery disease. According to our data, there is a direct relationship between the severity of coronary artery stenosis and the duration of diabetes. We also found a substantial relationship between the severity of coronary artery disease and the serum CRP level in people whose duration of diabetes is less than three years. In addition, in the 70- to 89-year-old age group, a meaningful relationship between the severity of coronary artery stenosis and serum CRP levels was observed.

Previous studies have shown that an increase in plasma CRP levels is associated with an increased risk of cardiovascular events among diabetic patients, independent of lifestyle, blood lipids, and glucose control. They found that there is a direct and significant linear relationship between increased hsCRP and the occurrence of cardiovascular events [7-11]. In a study by Claudia Lucci, et al. in 2020, they confirmed the presence of a close association between inflammation and DM status in acute myocardial infarction (AMI). Indeed, DM patients were more likely to have admission hs-CRP levels ≥ 2 mg/L and had a higher median hs-CRP value than non-DM patients. Moreover, both inflammation and DM status, considered separately, were predictors of in-hospital outcome and two-year mortality, even after adjustment for major confounders. Compared with our findings, they also found that hs-CRP predicts in-hospital outcomes and two-year mortality in AMI patients with and without DM. However, in DM patients, the same risk of developing events as in non-DM patients is associated with higher hs-CRP levels [12]. The findings by Farrokhian, et al. regarding the influence of chromium supplementation on metabolic status in patients with T2DM and coronary heart disease (CHD) showed that consuming chromium supplements

for 12 weeks led to a significant decrease in hs-CRP and plasma malondialdehyde (MDA) levels and a substantial increase in total antioxidant capacity (TAC) in diabetic individuals with CHD. They also revealed that in diabetic patients, oxidative stress and elevated inflammatory mediators such as CRP are associated with endothelial dysfunction and the progression of macrovascular disease [13]. The study by Liu Y, et al. assessed the predictive value of hs-CRP on admission, the severity of coronary artery lesions, and long-term outcomes in a large cohort of patients undergoing percutaneous coronary intervention (PCI). Similar to our study, this study declared that the level of hs-CRP was positively correlated with the severity of CAD and independently predictive of intermediate-high SYNTAX score (SS). This association was more significant in acute coronary syndrome (ACS) patients [14]. Sharif, et al. in their study, revealed that T2DM is associated with low-grade inflammation caused by adipose tissue dysfunction and insulin resistance. hs-CRP is a marker for systemic low-grade inflammation, and higher plasma levels have been associated with cardiovascular events in various populations. In patients with type 2 diabetes with and without manifest vascular disease, every 1 mg/l increase in plasma hs-CRP is related to a 21% increased risk of vascular mortality and a 26% increased risk of all-cause mortality. Plasma hs-CRP levels were not related to cardiovascular events in patients with type 2 diabetes mellitus, contrary to our findings [15]. Anwer, et al. Experimented to evaluate the role of hs-CRP in diagnosing and prognosis of ischemic heart disease and atherosclerosis. The study showed a highly significant linear correlation between hs-CRP and a syntax score of 15±10.52 and a clinical syntax score of 26.68 ± 12.17 [16].

Our study was not without limitations. The most important one was the descriptive nature of our study. Further clinical studies with long follow-up periods are recommended to establish our findings.

Conclusion

In this research, we aimed to evaluate the relationship between serum CRP level and the severity of coronary artery disease and the relationship between the duration of diabetes and the severity of coronary artery disease. According to our data, there is a direct relationship between the severity of coronary artery stenosis and the duration of diabetes. We also found a substantial relationship between the severity of coronary artery disease and the serum CRP level in people whose duration of diabetes is less than three years. In addition, in the 70- to 89-year-old age group, a meaningful relationship between the severity of coronary artery stenosis and serum CRP levels was observed. Therefore, elevated serum CRP levels may serve as a biomarker for assessing CAD risk in diabetic patients.

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