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Correlation of High Sensitive C-Reactive Protein with the Extent of Coronary Atherosclerotic Disease

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Abstract

Background and objectives: The inflammatory process of the intima of coronary vessels is significant in the atherosclerotic process. We aimed to evaluate the role of high sensitive C-reactive protein in diagnosing and prognosis of ischemic heart disease and atherosclerosis.

Methods: From 2021-2022, we randomly enrolled 100 patients referred to surgical specialty hospital/ cardiac center in Erbil City (Jan 2021- Jan 2022) for angiography complaining of a chronic coronary syndrome. Blood sampling was taken to measure (high sensitive C-reactive protein). Coronary artery angiography was done, and the extent of atherosclerosis was measured using the Syntax score and clinical syntax score using the calculator from internet site www.syntaxscore.org.

Results: We enrolled 58 males and 42 females; 39% of patients had Diabetes mellitus, 49% had hypertension, 41% were smoker, 18% with peripheral arterial disease, 8% had chronic obstructive disease, and 3% with left primary illness. The study showed a highly significant linear correlation between high sensitive C-reactive protein and syntax score of 15±10.52 and clinical syntax score 26.68±12.17.

Conclusion: The study concluded that a high sensitive C-reactive protein level is a reliable method to independently predict coronary artery disease in ischemic heart disease patients and the extent of severity; these results were not affected by sex category and other risk factors like diabetes mellitus, hypertension, or smoking.

Keywords: Atherosclerosis,High sensitive C-Reactive protein,Ischemic Heart disease**.**

Introduction

Ischemic heart diseases represent a considerable burden on both the individual & society.
Coronary heart disease (CHD) has been tremendously changing in the past 50years, with noticeable differences in its features between multi provinces of the world in many different regions. Mortality declined significantly in recent years;[1] thus, unexpectedly prevalence of CHD increased in USA and European countries, that is why the elderly are complaining more from CHD.

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While middle east CHD is still growing. Number of CHD patients is expected to increase in upcoming years, particularly in developing nations. CHD is a primary source of disability ; that's why it may be termed " disability-adjusted life years (DALYs).[1]

The atherosclerotic process is a continuous process leading to lipid accumulation in epicardial arteries forming vulnerable plaque and causing luminal narrowing. Lifestyle modification, pharmacological treatments, and interventional procedures will halt this process toward stabilization of the disease or regression of plaques. Various clinical scenarios are resulted from this continuous atherosclerotic process, either due to luminal narrowing called chronic coronary syndromes (CCS) or plaque rupture leading to acute coronary syndromes (ACS).[2].

The Pentraxin family of proteins has various members. The significant one is the C-reactive protein (CRP. They are mainly synthesized in the liver. Infections and inflammation trauma may lead to elevation of CRP. that is why any of these clinical conditions make serum CRP levels surge. Any increase beyond 10 mg/dl may be associated with the growth of erythrocyte sedimentation rates (ESR).[3] The HS- CRP is the most generally tested biomarker and is an ideal biomarker for global cardiovascular disease (CVD) risk assessment.[4] This was concluded from multiple studies done on the population; HS-CRP is classified by American Heart Association and Centers for Disease Control (AHA/CDC) as CVD markers of Global CVD into their levels <1, 1–3, and >3 mg/l as low risk, intermediate risk, high-risk groups, the binding capacity of CRP is attributed to numerous biological substrates,[5] all functions of CRP is attributed to its participation in the initiation of the complement system also modulation of function of phagocytic leukocytes. CRP is also located at sites of inflammation.[6] It enhances macrophage action on tumors[7] interleukine-1, tumor necrosis factor synthesis is also attributed to CRP. [8,] and platelet-activating factor is bonded and blocked by CRP. CRP synthesis by the liver as a reaction to interleukine-6. The SYNTAX score (SXscore) is a tool or a calculator used to grade the coronary arteries and the level of involvedness of coronary intima by atherosclerotic plaque; many studies showed its significance in predicting mortality and CAD level.[9] One of its limitations is that some clinical parameters are not involved while calculating the score, making it less accurate in predicting the prognosis.

To evaluate the severity of atherosclerotic plaques in CAD SYNTAX ("synergy between percutaneous coronary intervention with TAXUS and cardiac survey"), scores were measured by the SYNTAX website (http://www.syntaxscore.org).

Correspondingly any coronary lesion ≥50% in diameter in each artery ≥1.5 mm was counted by the standard score system. The net scores were summated as the SYNTAX score (SYNTAX score calculator 2021). SYNTAX score equal to 0 refers to the absence of CAD, or the presence of a 1 refer to plaque of ≥50% narrowing in any coronary vessel. Clinical SYNTAX Score CSS is a modified syntax score that adds multiple clinical factors like Age, creatinine clearance CrCl, left ventricular function LVEF, presence of left central disease (LM), presence of peripheral vascular disease (PVD), gender, in addition to anatomical syntax score Calculating clinical syntax score by adding the parameters through the website calculator.[10] This study aims to evaluate the role of high sensitive C-reactive protein in the diagnosis and prognosis of IHD and atherosclerosis process.

Patient and methods

The conducted study sample is 100 patients collected between the period from jan 2021 – jan 2022. These patients complained from chronic coronary syndrome (chest pain and or dyspnea on exertion). The sample collected randomly in the cardiac center of Erbil city, and blood sample withdrawn. The high-sensitive C-reactive protein test and coronary arteries angiography done.

Syntax score (1) and clinical syntax score (2) had been measured from angiography cine results using the site www.syntaxscore.com this site is a standard calculator that used to estimate the severity of coronary artery disease by choosing the number of vessel affected and location, complexity ,calcification bifurcation long diffuse lesion and accordingly with give us a number represent the level of disease extent .then clinical syntax score measured which a combination of syntax score plus multiple clinical parameter such as (age ,gender, creatinine clearance, COPD, Left ventricular Ejection Fraction LVEF, peripheral arterial disease PD). Creatinine clearance (CrCl) was calculated using the Cockcroft-Gault equation.[11] The ejection fraction of the left ventricle (LVEF) was estimated by echocardiography before angiography. The patients are classified into groups according to their syntax score and clinical syntax score CSS low risk group (CSS $\leq$ 15.6), CSS intermediate group (15.6 < CSS < 27.5), CSS high group (CSS $\geq$ 27.5. complete History from the patients was taken, and a forum was filled about History of hypertension, diabetes, smoking, and leg claudication. Several Categorical variables will be stated as (%), and mean ± SD are expressed as continuous variables. They used an independent sample t-test and ANOVA to compare the mean values by groups. Correlation analysis using Linear regression, describing it as Pearson correlation coefficients. Multivariate linear, independent determinants, and linear correlations will be used for the study of models based on the stepwise range will be generated for variables that showed. Statically significant is regarded as any p-value < 0.05. For all tests, software (SPSS version 26.0; SPSS, Inc., Chicago, IL, USA) will be used for analyses. Patients with congenital, rheumatic, pulmonary, and thromboembolic heart disease were excluded, and patients with acute coronary syndrome or heart failure were banned. Any infection or allergic illness was excluded. All Information was explained to the participants, including how the study to be done and blood tests to be taken from them, Informed consent was taken. Patients are reassured that their Information is confidential and nothing will be published without their permission. This work has been approved by the research ethics committee at Hawler Medical University.

Results

This study included 100 patients with a mean age of 56.48±8.966 years. The majority of the patients were male (58%), female (42%), there was 39% Diabetic, and 61% nondiabetic shown,(49%) had hypertension (HTN), (41%) smoker shown,(18%) with peripheral arterial disease (PD), (8%) with chronic obstructive disease COPD,(3%) with Left central disease (LM).

The correlation matrix shows that High sensitivity is significantly positively correlated with Syntax score (r = .882, p<.01), Table (1).

Table (1): Correlation analysis Syntax score and High sensitive CRP (HS-CRP)

	Mean	Std. Deviation	N
Hs-crp	4.3042	5.07879	100
syntax score	15.33	10.526	100

Correlations			
		Hs-crp	syntax score
Hs-crp	Pearson Correlation	1	.882**
	Sig. (2-tailed)		.000
	N	100	100
syntax score	Pearson Correlation	.882**	1
	Sig. (2-tailed)	.000	
	N	100	100

After doing correlation matrix shows that Hs-CRP is significantly positively correlated with extroversion (r = .632, p<.01), Table (2).

Table(2).correlation between Hs-crp and clinical syntax score correlations

		Hs-crp	Clinical syntax score PCI
Hs-crp	Pearson Correlation	1	.632**
	Sig. (2-tailed)		.000
	N	100	100
Clinical syntax score	Pearson Correlation	.632**	1
	Sig. (2-tailed)	.000	
	N	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

Anova analysis showed a highly significant correlation between syntax risk groups in correlation with HS-SRP (P < 0.0001), Table (3).

Table (3). Correlation between HS-CRP and syntax score groups

Hs-CRP	Descriptive Statistics							
					95% Confidence Interval for Mean			
	N	Mean	Std. Deviation	Std. Error	Lower Bound	Upper Bound	Minimum	Maximum

Low risk	59	1.1602	.92603	.12056	.9188	1.4015	.01	4.18
Intermediate risk	23	5.9770	3.53385	.73686	4.4488	7.5051	2.15	14.00
High risk	18	12.4722	4.73209	1.11537	10.1190	14.8254	6.51	21.81
Total	100	4.3042	5.07879	.50788	3.2965	5.3119	.01	21.81

HS-CRP

Correlations

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1848.466	2	924.233	127.137	.000
Within Groups	705.150	97	7.270		
Total	2553.616	99			

The correlation matrix shows that Hs-CRP is significantly negatively correlated with ejection fraction ($r = -.717$, $p<.01$), table (5) chi-square analysis shows a non-significant correlation between gender with HS-CRP. Table (4).

Table (4). Correlation between Hs-CRP and ejection fraction

Correlations

		Hs-CRP	ejection fraction
Hs-crp	Pearson Correlation	1	-.717**
	Sig. (2-tailed)		.000
	N	100	100
ejection fraction	Pearson Correlation	-.717**	1
	Sig. (2-tailed)	.000	
	N	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

We found a non-significant difference in high-sensitive CRP correlation in gender category between males and females p value =0.2. Table (5).

Table (5). Correlation in sex categories with HS-CRP

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	3.156[a]	2	.206	.227		
Likelihood Ratio	3.287	2	.193	.219		
Fisher's Exact Test	3.152			.218		
Linear-by-Linear Association	.522[b]	1	.470	.518	.278	.080
N of Valid Cases	100					

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 7.56.
b. The standardized statistic is -.722.

Discussion

CAD is a leading cause of mortality, morbidity, and disability. Moreover, it has been associated with several risk factors. This study shows a highly significant linear correlation between highly sensitive CRP and syntax score and clinical syntax score as expected from the research plan this was constant with another study done in Saudi Arabia of about 100 patients in which Habib and colleagues found higher level of HS-CRP in patient with advanced level of atherosclerosis,[12] which was also what Ozdemir found that CRP level is associated with syntax score current study focused on high sensitive CRP in correlation with syntax score and clinical syntax score in which he concluded that inflammation is a significant part of the atherosclerotic process that lead to elevation of CRP,[13] clinical syntax score which does ad-on syntax score and strengthens the accuracy and positive predictive value of the test. These clinical factors are Age, creatinine clearance, Left primary Disease (LM), Left ventricular Function (EF), gender, Chronic obstructive pulmonary disease (COPD), and Peripheral vascular Disease (PVD). Furthermore, The SS refers to the amount and severity of the coronary lesions, thus defining the myocardium underneath the jeopardy of ischemia. Several syntax trials established that SS was an independent prognosticator of short-and long-term morbidity and mortality, as well as adverse cardiovascular outcomes in a wide range of patients, including stable CAD.[14-16] The present study showed a highly significant difference in High sensitive CRP levels between the low, intermediate, and high-risk groups of atherosclerosis disease demonstrated by syntax score and clinical syntax score. Those patients with a high degree of syntax scores are often treated with coronary artery bypass surgery (CABG) had high degrees of HS-CRP. This goes with what Dr Akopoulou found in his study .Inflammation act an essential part in all phases of atherosclerosis;[17] it also goes with

what Garg found in his study;[16] subsequently highly sensitive CRP is commonly used in daily practice as a marker of inflammation. HS-CRP, an acute-phase protein from the liver, is elevated in reaction to inflammation and enhances risk expectations for patients with CAD,[18] this study found that high HS-CRP levels are related to the complexity of coronary lesions in patients with stable CAD. Liu Y also approved this in an extensive survey of about 10000 patients done in 2013.[18.] Another important correlation in this study shows a significant paradoxical correlation between HS-CRP and ejection fraction. This finding is precious for risk stratification patients with HF with reduced ejection fraction. These results came comparable with studies that found Zohair in his research. He studied 227 patients in Alriadh hospital and showed a significant inverse relationship between HS-CRP and Ejection fraction post-myocardial infarction.[19] various factors may be interrogated, another finding in the current study is shown was a non-significant difference in high-sensitive CRP correlation in gender category which makes this test applicable in both sexes with high sensitivity this goes with what Chiriboga and[21] Musunuru studies revealed that HS-CRP an independent risk factor for CAD of sex category in intermediate risk of an asymptomatic patient for Coronary artery diseases [22].

Conclusion & Recommendations:

We conclude that High sensitive CRP level is a reliable method to predict CAD in IHD patients in an independent manner not affected by sex category and all other risk factors. We also concluded that inflammatory process Has an essential role in CAD process, we recommend further research on the effect of revascularization on the level OF HS-CRP.

Limitations: the limited number of patients and single-center study.

Conflict of Interest

The authors had nothing to declare.

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