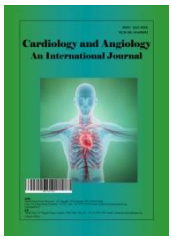

Cardiology and Angiology: An International Journal

11(4): 113-119, 2022; Article no.CA.84249
ISSN: 2347-520X, NLM ID: 101658392

Highly Sensitive C Reactive Protein as a Predictor of in Hospital Outcome in Patients with Acute Coronary Syndrome

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/CA/2022/v11i430213

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/84249

Original Research Article

Received 05 February 2022
Accepted 11 April 2022
Published 08 June 2022

ABSTRACT

Background: C-reactive (CRP) protein is a well-studied inflammatory factor whose prognostic value in cardiovascular diseases in recent years has become increasingly important. Assesses of prognostic value of highly sensitive C-reactive protein (hs-CRP) in patients with acute coronary syndrome (ACS) wasthe aim of this work.
Methods: This observational research was conducted on 50 individuals had ACS admitted to CCU and indicated for invasive coronary angiography. Cases were classified in 2 groups depending on the level of hs-CRP: group A included (14) cases with hs-CRP > (2) and group B involved (36) cases with hs-CRP ≥ (2). All patients were subjected to: laboratory investigations (creatinine, urea, aspartate aminotransferase (AST), alanine amino transferase (ALT), troponin, creatine kinase myocardial band (CKMB), hs-CRP, HbA1C, lipid profile, twelve lead surface ECG, echocardiography and coronary angiography.
Results: Total cholesterol, LDL, HDL and triglyceride were significantly higher in group B compared to group A(P=0.001). Stent implantation was significantly higher in group 2 compared to group 1 (P=0.040)
Conclusions: There were correlation between hs CRP and lipid profile as a risk factor and there was no correlation between in hospital outcome and hs CRP in ACS patients due to small sized study.

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Keywords: Highly sensitive; c reactive protein; hospital outcome; acute coronary syndrome.

1. INTRODUCTION

Inflammatory biomarkers provide useful insight into the atherosclerosis inflammatory process; they operate as a window into the cell activation process, inflammatory cells recruitment, and proliferation [1].

Despite significant advancements in pharmacological and interventional therapy, acute coronary syndrome (ACS) continues to be the leading cause of morbidity and mortality in the modern world. [2]. Inflammation plays a critical role in the initiation and promotion of atherosclerotic lesions and can stimulate ACS by plaque instability induction. C-reactive protein (CRP) is a well-studied inflammatory factor with a growing predictive significance in cardiovascular illnesses in recent years.

[3-8]. "Additionally, CRP is no longer merely considered a marker but also recognised as an atherosclerosis mediator" [9,10].

"Earlier in ACS, a high level of highly sensitive C-reactive protein (hs-CRP), before myocardial necrosis development, is an indicator which is important for poor prognosis with cardiovascular comorbidities. Its evaluation during the ACS time course may aid in myocardial dysfunction risk stratification" [11].

"American Heart Association (AHA) and Centre for Disease Control (CDC) produced a scientific statement) in which hs-CRP has mentioned as the only inflammatory marker that can be utilised for risk prediction both for primary and secondary prevention of cardiovascular events" [7]. The aim of this work was to assess prognostic value of hs-CRP in ACS patients.

Patients and Methods: This observational research was conducted on 50 cases with ACS admitted to CCU and indicated for invasive coronary angiography, who had unstable angina, ST elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (NSTEMI).

Patients with chronic renal disease, chronic liver diseases, acute or chronic inflammation, pregnancy, malignancy, pervious PCI and CABG were excluded.

All patients were subjected to: full history taking, clinical examination (vital signs, signs of inflammation, autoimmune diseases as systemic lupus and rheumatoid arthritis), laboratory investigations (creatinine, urea, aspartate aminotransferase (AST), alanine amino transferase (ALT), creatine kinase myocardial band (CKMB), troponin, hs-CRP), HbA1C, lipid profile (triglyceride, total cholesterol, LDL-C and HDL-C), twelve lead surface ECG, echocardiography and coronary angiography.

Twelve lead surface ECG: ST-segment elevation is considered suggestive of continuing acute occlusion of coronary artery in the following situations: two contiguous leads at least with ST-segment elevation ≥ 2.5 mm in men < 40 years, ≥2 mm in men ≥ 40 years, or ≥ 1.5 mm in women in leads V2–V3 and/or ≥ 1 mm in the other leads. It is advised that patients with inferior MI have their right precordial leads (V3R and V4R) recorded for ST-segment elevation to determine concomitant infarction of right ventricular (RV). ST-segment depression in leads V1–V3 suggests myocardial ischaemia, especially when the terminal T-wave is positive (ST-segment elevation equivalent), and confirmation by concomitant ST-segment elevation ≥ 0.5 mm recorded in leads V7–V9 should be considered as a means to identify posterior MI. Non-ST-segment elevation ACS exhibit ECG changes that may include transient ST-segment elevation, persistent or transient ST-segment depression, T-wave inversion, flat T waves or pseudo-normalization of T waves or the ECG may be normal.

Echocardiography: Transthoracic Echocardiography will be performed to assess the presence or absence of mechanical complications and the overall systolic function. The ejection fraction is measured using modified Simpson's method in apical [4,2].

Coronary angiography: According to American Heart Association (AHA), The procedure is done in a hospital cardiac catheterization lab: a local anaesthetic is usually given to numb the needle puncture site. we will make a needle puncture through your skin and into a large blood vessel. A small straw-sized tube (called a sheath) will be inserted into the vessel. The doctor will gently guide a catheter (a long, thin tube) into your vessel through the sheath. A video screen will show the position of the catheter as it is threaded through the major blood vessels and to the heart. When a catheter is used to inject a dye that can

be seen on X-rays, the procedure is called angiography. When a catheter is used to clear a narrowed or blocked artery, the procedure is called angioplasty or a percutaneous coronary intervention (PCI).

2.1 Criteria of STEMI, NSTEMI and Unstable Angina

Chest pain: is the hallmark of myocardial ischemia and it especially pronounced in patients with acute STEMI, the reason symptoms are more severe in patients with STEMI as compared with NSTEMI and unstable angina.

ECG: STEMI is defined by the presence of significant ST segment elevation, pathological Q waves and reciprocal ST segment depression. NSTEMI is defined by the absence of ST segment elevation, presence of ST segment depressions and/or T wave inversions such as unstable angina.

Cardiac enzymes: STEMI, NSTEMI will exhibit elevated troponin levels. Those who do not display elevated troponin levels are classified as unstable angina.

2.2 Statistical Analysis

The data was collected, edited, coded, and entered into the IBM SPSS version 20 statistical package for social science. When the distribution of qualitative data was determined to be parametric, it was provided as a number and a percentage, whereas quantitative data was presented as a mean, standard deviations, and ranges. When the predicted count in any cell was less than 5, the Chi-square test and/or Fisher exact test were employed instead of the Chi-square test to compare two groups with qualitative data. The independent t-test was used to compare two independent groups with quantitative data and parametric distribution. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant if $P < 0.05$.

3. RESULTS

Gensini score was significantly higher in group B compared to group A (P=0.001). Demographic data, smoking, HTN and diabetes was insignificantly different between two groups. [Table 1].

Total cholesterol, LDL, HDL and triglyceride were significantly higher in group B compared to group A(P=0.001). Urea, creatinine, ALT, AST, HbA1c and LVEF were insignificant difference between the two groups [Table 2].

Stent implantation was significantly higher in group 2 compared to group 1 (P=0.040). Incidence of unstable angina, NSTEMI, STEMI, death, cardiogenic shock, acute pulmonary edema, atrial fibrillation, mechanical ventilation, ventricular fibrillation and ventricular tachycardia were insignificantly different between the two groups [Table 3].

Table 1. comparison between two groups according to demographic data, Gensini score, smoking, HTN, diabetes

		Group A(n=14)	Group B(n=36)	t. test	p. value
Age		48.07±4.81	46.08±6.59	1.025	0.311
Sex	**Male**	7(50%)	19(52.8%)	0.031	0.860
Weight		72.79±9.16	70.25±8.34	0.939	0.352
Height		1.60±0.12	1.60±0.10	0.002	0.998
BMI		28.69±4.99	27.51±3.57	0.932	0.356
Gensini score		30.29±18.62	80.28±52.35	3.470	0.001*
				X^2	**P-value**
Smoking		8 (57.1)	15(41.7)	0.972	0.324
HTN		11 (78.6)	22 (61.1)	1.369	0.242
Diabetes		7(50.0)	26 (72.2)	2.218	0.136

Data are presented as mean ± SD or frequency (%), BMI: Body mass index, HTN: hypertension

Table 2. Shows comparison between two groups according to demographic data of Urea, Creatinine, ALT, AST, total cholesterol, LDL, HDL, triglyceride, HbA1c and LVEF

	Group A	Group B	t. test	p. value
Urea	20.07±7.26	22.03±6.91	0.886	0.380
Creatinine	0.94±0.15	0.93±0.19	0.312	0.756
ALT	15.93±2.92	17.00±3.94	0.921	0.362
AST	16.93±2.56	16.56±3.18	0.392	0.697
Total cholesterol (mg/dL)	87.77±47.34	174.04±40.90	6.409	0.001*
LDL-C, (mg/dL)	51.20±27.71	112.22±29.00	6.760	0.001*
HDL-C, (mg/dL)	27.74±17.93	53.61±20.54	4.134	0.001*
Triglyceride, (mg/dL)	86.25±49.52	166.56±78.44	3.552	0.001*
HbA1c (NGSP), %	7.34±1.47	7.56±1.56	0.451	0.654
LVEF, %	60.57±13.78	57.69±15.31	0.614	0.542

*Alt: Alanine transaminase, AST: Aspartate aminotransferase, LDL: Low density protein, HDL: High density protein, HbA1c: Hemoglobin A1c, LVEF: Left ventricular ejection fraction, *: significant P value*

Table 3. comparison between two groups according to the incidence of unstable angina, NSTEMI, STEMI, death, cardiogenic shock, acute pulmonary edema, atrial fibrillation, mechanical ventilation, ventricular fibrillation, ventricular tachycardia and stent implantation

	Group A	Group B	X^2	P-value
Unstable angina	5(35.7%)	14(38.9%)	0.043	0.836
NSTEMI	2(14.3%)	9(25.0%)	0.674	0.412
STEMI	6(42,8%)	14(38.9%)	0.511	0.066
Death	3(21.4%)	2(5.6%)	2.822	0.093
Cardiogenic shock	5(35.7%)	7(19.4%)	1.463	0.226
Acute pulmonary edema	5(35.7%)	7(19.4%)	1.463	0.226
Atrial fibrillation	2(14.3%)	8(22.2%)	0.397	0.529
Mechanical ventilation.	3(21.4%)	4(11.1%)	0.891	0.345
Ventricular fibrillation	6(42,8%)	9(25.0%)	1.531	0.216
Ventricular tachycardia	4(28.6%)	9(25.0%)	0.067	0.796
Stent implantation	1(7.2%)	13(36.2%)	4.196	0.040*

*X^2: Chi square test, *: significant P value, STEMI: ST-elevation myocardial infarction.*

4. DISCUSSION

Numerous biomarkers have been identified as being related with the initiation and progression of coronary heart disease. Historically, the function of hs-CRP as a risk factor for cardiovascular disease was controversial. [12].

The results of the present research are comparable to the studies by Cavusoglu Y, et al [13] And Tomoda N, et al. [14] who reported that the concentrations of CRP in ACSs patients , within 6 hours of symptoms onset were significantly higher in comparison to the Control Group. The process of inflammation has been proved to be one of the mechanisms causing rupture of plaque leading to elevated levels of CRP in less than 6 hours in ACS patients. In ACS patients, concentrations of hsCRP are more than 10-fold higher than in patients with stable coronary disease or no known coronary disease.

Research by Vasan et al. [15] compared between heart failure and hsCRP in patients with STEMI and Mega et al 103. Study that confirmed the presence of an connection between heart failure and hsCRP when these variables were used as a part of a composite endpoint in ACS patients as in Sabatine et al., [16] and Varo et al., [17] studies.

While Mach et al., [18] reported that among acute ischemic heart disease patients and no biological markers of myocardial necrosis, the concentration of CRP at the admission time was significantly higher in patients in ultimately diagnosed with acute myocardial infarction , while in patients with unstable angina the levels of CRP were low.

On the other hand, Bogaty et al., [19] reported that assessment of severity of atherosclerosis through using only the Gensini score as grading

tool showed that hsCRP levels correlated with the severity of atherosclerosis.

"Elevated CRP concentration in patients who presented to hospital with chest pain due to ACS was previously demonstrated" by others Niccol et al., [20]. and Arroyo et al., [21].

Ray et al., [22] concluded that "the addition of hsCRP to lipid-based measurements significantly improved risk prediction, in contrast, other studies showed lower discriminative usefulness of CRP 111"."Also, hsCRP levels after AMI predicted emergence of heart failure in a study by Stumpf et al., [23] and also found that peak CRP is also a strong predictor of global and cardiovascular mortality during the following year after STEMI."

Bursi et al., [24]. reported in "a recent study that CRP at admission to hospital is useful for predicting the time course of heart failure in patients with AMI". The study by Kavsak et al., [25]. Indicated that "high CRP titers, independent of the subjects' age, gender, and cTnI concentrations, predict long-term heart failure and mortality".

Morrow et al., [26] that study "used a cut off of 1.5 mg/dl (similar to ours) and observed that elevated CRP at admission was associated with higher mortality at 14 days". Schoos et al., [27] demonstrated that "pre-procedures CRP is an independent and strong predictor of a composite endpoint of death, nonfatal recurrent myocardial infarction, and stent thrombosis after percutaneous intervention with coronary stent implantation [28] confirmed the prognostic value of CRP in predicting short- and long-term outcomes after ACS".

Limitations: Its small sized study and done in one centre, a large study on a large number of populations in multiple centres is needed to validate the results.

5. CONCLUSIONS

There was a correlation between hs CRP and lipid profile as a risk factor and there was no correlation between hs CRP and in hospital outcome in ACS patients due to small sized study.

CONSENT AND ETHICAL APPROVAL

The research was done after approval from the Ethical Committee Tanta University Hospitals. An informed written consent was obtained from the patient.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
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