



Role of High Sensitivity C-Reactive Protein (HS-CRP) as a Predictive Marker for Coronary Heart Disease Compared to Troponin I Disease in Sudanese Patients in Khartoum State.

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Abstract

Background: Heart disease may be a leading cause of death, but that do not mean we have to accept it as fate. Although many risk factors may appear to be as an earlier predictor for cardiac disease — such as family history, sex or age — but the laboratory and clinical evaluations are very important to have the final word.

Measurement of inflammatory markers as high-sensitivity C-reactive protein (HS-CRP) may provide a novel method for detecting individuals at high risk of plaque rupture. Several large-scale prospective studies ⁽¹⁾⁽²⁾⁽³⁾ considered that HS-CRP is a probable independent predictor of future myocardial infarction and stroke among apparently healthy men and women and that the addition of HS-CRP to standard lipid screening may improve global risk prediction among those with high as well as low cholesterol levels.

Objectives: To measure the High Sensitivity C-reactive protein (hs-CRP) in serum of patients with cardiac diseases and in serum of individuals with risks of cardiac diseases and compare with troponin I.

Material and methods: The study was conducted in Khartoum state, Sudan. The samples were taken from intensive care unit (ICU) of many hospitals including Khartoum teaching hospital, Khartoum North teaching hospital, Omdurman teaching hospital, Ahmed Gasim teaching hospital, Sudan Cardiac Center and International hospital. After informed consent was obtained, 300 subjects were included in this study. 150 patients were known with chronic heart disease (CHD) (positive control group), while, 100 volunteers were carefully picked out to be under suspicious of CHD and 50 healthy volunteers were selected as control (negative control group). Data was analysed using SPSS Version 22 software. P value < 0.05 was considered as statistically significant.

Results: In this study, the results of High Sensitivity C-reactive protein (hs-CRP) were significantly different in (p-value = 0.000) in coronary heart disease (CHD) subjects as compared to healthy controls and risk group. Mean levels of hs-CRP in CHD subjects, risk and healthy controls were 12.13 ±2.26 mg/L, 4.17±1.26 mg/L and 0.74±0.13 mg/L respectively

Key words: High sensitivity C-reactive protein (hs-CRP), Troponin I, CHD.

Introduction

Introduction and Literature review

Inflammation plays a role in the development of atherosclerosis and coronary heart disease. Elevated markers of inflammation, in particular CRP, are associated with an increased risk of future cardiovascular events in healthy subjects, in patients with stable or unstable coronary artery disease and acute myocardial infarction (4). The most common cause of coronary heart disease is atherosclerosis with erosion or rupture of a plaque causing transient, partial or complete arterial occlusion. Heart cannot continue to function without adequate blood flow, and if it is severely compromised, death is inevitable. Several risk factors for coronary heart disease have been well documented, including hypertension, hyperlipidemia, diabetes, a positive family history of CHD, smoking, obesity and physical inactivity (5).

Highly sensitive CRP (Hs-CRP):

C-reactive protein (CRP) is the prototype acute-phase protein primarily synthesized in the liver and its release is stimulated by interleukin 6 (IL-6) and other pro inflammatory cytokines (5). Composed of five 23 kDa subunits, C-reactive protein (CRP) is a hepatically derived pentraxin that plays a key role in the innate immune response. CRP has a long plasma half-life and is now understood to be a mediator as well as a marker of atherothrombotic disease. Highly sensitive CRP (Hs-CRP) has been shown to have prognostic value in patients with acute coronary syndromes; however, the most promising use of Hs-CRP has been in the primary prevention setting. Hs-C-reactive protein not only may be a marker of low grade chronic systemic inflammation but also may be directly involved in atherosclerosis (6). It can amplify the anti-inflammatory response through complement activation of endothelial cells (7). In the present communication, we assessed the high sensitivity C-reactive protein in patients with coronary heart disease with age and sex matched healthy subjects. It has recently been suggested that a marker of inflammation, along with serum cholesterol, may be critical component in the development and progression of atherosclerosis (8)(9).

A growing body of evidence has supported the idea that cardiovascular diseases including coronary heart disease, ischemic stroke, and acute myocardial infarction, develop, at least in part, because of a chronic low-level CRP of the vascular endothelium (10)(11).

Apparently, high-sensitivity CRP (hsCRP) is emerging as the strongest and most independent predictive risk factor for atherosclerosis and cardiovascular diseases (CVD) (7)(9). American Heart

Association (AHA) and Centers for Disease Control and Prevention (CDC) issued a statement regarding use of C-reactive protein to assess risk of cardiovascular diseases. For people without an overt inflammatory disease, cardiovascular risk assessment cutoffs have been recommended as follows:

- If Hs-CRP level is lower than 1.0 mg/L, a person has a low risk of developing cardiovascular disease.
- If Hs-CRP is between 1.0 and 3.0 mg/L, a person has an average risk.
- If Hs-CRP is higher than 3.0 mg/L, a person is at high risk.

A growing number of studies have examined whether hs-CRP can predict recurrent cardiovascular disease, stroke and death in different settings. High levels of hs-CRP consistently predict recurrent coronary events in patients with unstable angina and acute myocardial infarction (heart attack). Higher hs-CRP levels also are associated with lower survival rates in these patients. Many studies have suggested that after adjusting for other prognostic factors, hs-CRP is useful as a risk predictor. The high-sensitivity C-reactive protein (hs-CRP) assay is a quantitative analysis test of very low levels of C-reactive protein (CRP) in the blood. The hs-CRP assay is being increasingly used as a marker for cardiac risk assessment and as a prognostic tool in heart disease

Clinical Applications

Hs-CRP in Atherosclerosis and Plaque Instability/Inflammation:

With the recognition of the crucial link between arterial damage, inflammatory processes, and coronary atherosclerosis, hs-CRP estimation has assumed a vital role in cardiac risk assessment. C-reactive protein is an important pathogenic factor for atherosclerosis and induces several reactions involved in atherothrombogenesis:

- Activates complement and attacks monocytes
- Incites endothelial dysfunction
- Augments a procoagulant state
- Contributes to plaque instability/rupture

Hs-CRP in Risk Stratification and Risk Assessment:

Hs-CRP levels help in cardiac risk stratification and assessment, and it are a key prognostic factor in conditions such as

- Acute coronary syndrome (ACS)
- Stroke
- Peripheral artery disease (PAD)
- Post-MI complications such as cardiac failure

High Sensitivity (also called Ultra-sensitive) C-reactive protein is known as HS-CRP, US-CRP or CRP for short. It is a protein found in the blood and what we call a "marker" for inflammation, meaning its presence indicates a heightened state of inflammation in the body. Inflammation is a normal response to many physical states including fever, injury and infection. Inflammation plays a role in the initiation and progression of cardiovascular disease.

Troponin

It has been known for 50 years that transaminase activity increases in patients with acute myocardial infarction. With the development of creatine kinase (CK), biomarkers of cardiac injury began to take a major role in the diagnosis and management of patients with acute cardiovascular disease. In 2000 the European Society of Cardiology and the American College of Cardiology recognized the pivotal role of biomarkers and made elevations in their levels the “cornerstone” of diagnosis of acute myocardial infarction. At that time, they also acknowledged that cardiac troponin I and T had supplanted CK-MB as the analytes of choice for diagnosis. In this review, we discuss the science underlying the use of troponin biomarkers, how to interpret troponin values properly and how to apply these measurements to patients who present with possible cardiovascular disease (12).

Materials and Methods

Study Design

This study was across sectional observation study to detect possibility of high sensitivity C-reactive protein (hs-CRP) as a predictive marker for coronary heart disease compared to Troponin I.

Study area

The study will be conducted in Khartoum state, Sudan. The samples were taken from intensive care unit (ICU) of many hospitals including Khartoum teaching hospital, Khartoum North teaching hospital, Omdurman teaching hospital, Ahmed Gasim teaching hospital, Sudan Cardiac Center and International hospital.

Study Group

The study was conducted in Khartoum state, Sudan. The samples were taken from intensive care unit (ICU) of many hospitals including Khartoum teaching hospital, Khartoum North teaching hospital, Omdurman teaching hospital, Ahmed Gasim teaching hospital, Sudan Cardiac Center and International hospital. After informed consent was obtained, 300 subjects were included in this study. 150 patients were known with chronic heart disease (CHD) (positive control group), while, 100 volunteers were carefully picked out to be under suspicious of CHD and 50 healthy volunteers were selected as control (negative control group).

Inclusion Criteria

Participants with chronic heart disease (CHD) (positive control group), while, 100 volunteers were carefully picked out to be under suspicious of CHD and 50 healthy volunteers were selected as control (negative control group).

Exclusion Criteria

The volunteers who refused to participate in the study were excluded. Patients with renal failure, any sort of infection, autoimmune disease, cancer and pregnancy were excluded too from this study.

Ethical considerations: An ethical clearance of this study was approved by the ethical committee of Omdurman Islamic University. Informed consent was obtained from each participant before taking the samples.

From each volunteer 7 ml blood sample was taken using standard venipuncture technique in vacutainer tubes. The samples were distributed into plain container (for hs-CRP) and in EDTA container (for troponin I).

Quality controls and managements: Blood was collected with care and adequate safety precautions to ensure test results were reliable. Quality Assurance (QA) and standard Operating System was followed for all biological and clinical tests to achieve validity and reliability of test results.

Methods of BMI estimation:

It calculates a value indicative of the fat content of the body by dividing the weight by the square of height

$$BMI = \frac{\text{mass(kg)}}{(\text{height(m)})^2}$$

BMI Categories:

Categories	BMI
Underweight	Less than 18.5
Normal weight	18.5 – 24.9
Overweight	25 – 29.9
Obese	30 or higher

Statistical Analysis Statistical Analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0.(Armonk, NY: IB was M Corp)Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level. Chi-square test was used for categorical variables, to compare between different groups.Student t-test.was used for normally distributed quantitative variables, to compare between two studied groups .F-test (ANOVA) was used for normally distributed quantitative variables, to compare between more than two groups, and Post Hoc test (Tukey) (LSD) for pairwise comparisons.Pearson coefficient to correlate between two normally distributed quantitative variables .Mann Whitney test was used for abnormally distributed quantitative variables, to compare between two studied groups .Kruskal Wallis test was used for abnormally distributed quantitative variables, to compare between more than two studied groups, and Post Hoc (Dunn's multiple comparisons test) for pairwise comparisons.

Results

Blood samples were collected from volunteers via venipuncture in fasting state.

In this study, the results of High Sensitivity C-reactive protein (hs-CRP) were significantly different in (p-value = 0.000) in coronary heart disease (CHD) subjects as compared to healthy controls and risk group.

Mean levels of hs-CRP in CHD subjects, risk and healthy controls were 12.13 ± 2.26 mg/L, 4.17 ± 1.26 mg/L and 0.74 ± 0.13 mg/L respectively (table 1-1, fig. 1-1). These observations in table 3-1 imply that a subclinical inflammatory reaction has a role in atherosclerosis in coronary heart disease as shown.

Comparison of mean Serum Troponin I in between healthy controls, risk and CHD subjects was significant (p-value =0.000). Mean value of serum Troponin I in between healthy controls was 0.80 ± 0.05 mg/dl, risk was 0.06 ± 0.02 mg/dl and CHD subjects was 3.34 ± 1.86 mg/dl respectively (table 1-1, fig1-2).

		N	Mean	Std. Deviation	P-value
Hscrp	Case	150	12.13	2.26	0.000
	Risk	100	4.17	1.26	
	Control	50	0.74	0.13	
	Total	300	7.58	5.02	
TroponinI	Case	150	3.34	1.86	0.000
	Risk	100	0.06	0.02	
	Control	50	0.08	0.05	
	Total	300	1.71	2.10	

Table (1-1): Comparison the mean level of Hs-crp and TroponinI between risk, control and CHD groups.

	Status	N	Mean	Std. Deviation	P-value
Hscrp	Risk	100	4.2	1.3	0.000
	Control	50	0.7	0.1	
TroponinI	Risk	100	0.1	0.0	0.10
	Control	50	0.1	0.0	

Table (1-2): Comparison the mean level of Hs-Crp and Troponin I between risk and control groups

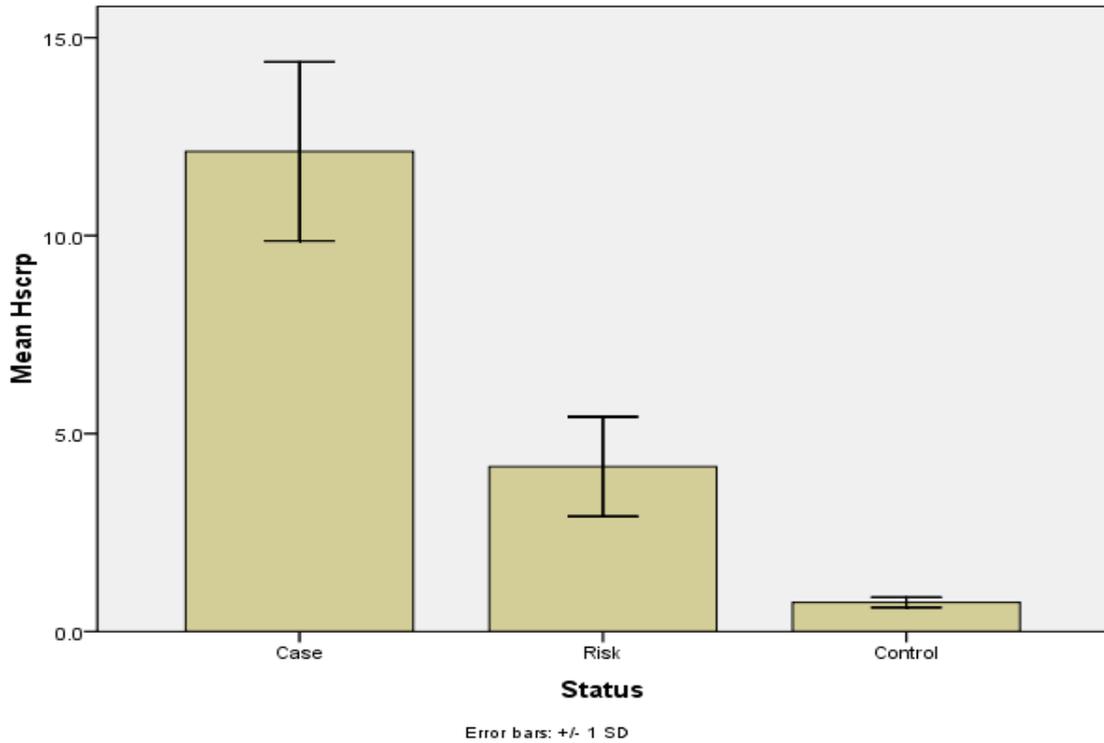


Figure (1-1): The mean level of Hs-crp in all groups

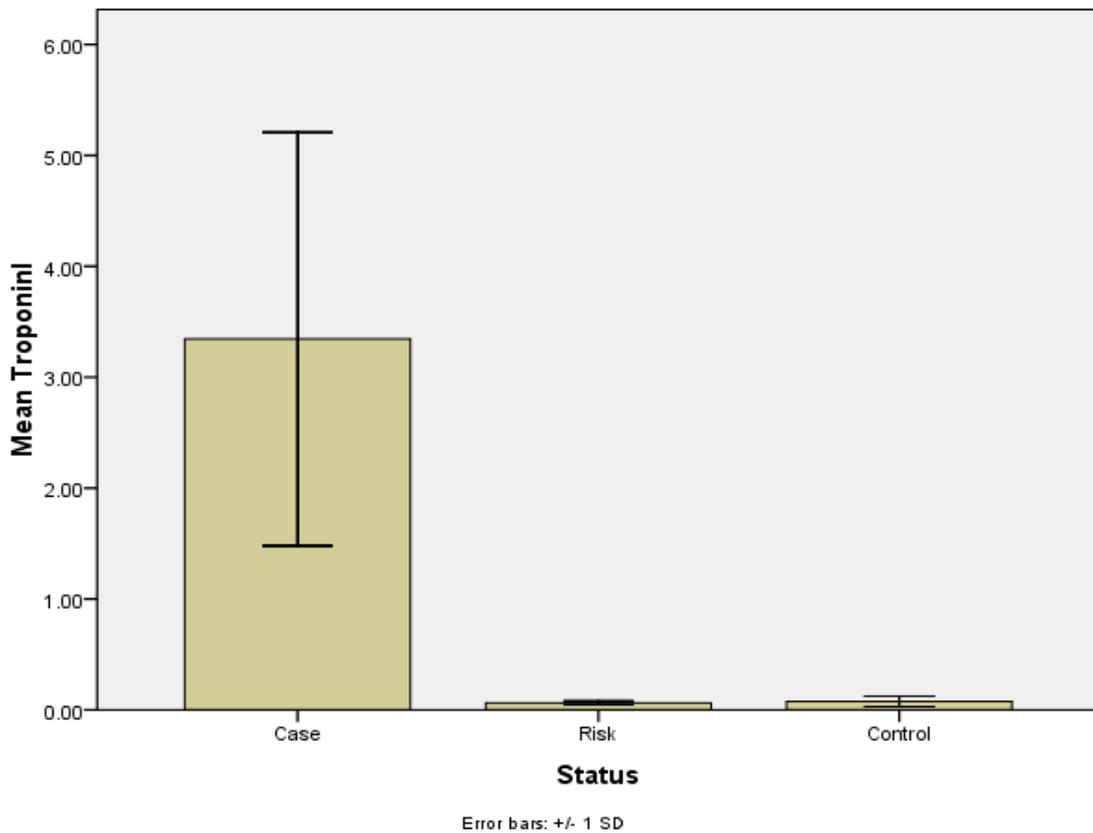


Figure (1-2): The mean level of troponinI in all groups

Age	N	Mean	Std. Deviation	P- value
40 – 49	3	11.33	1.15	0.885
50 – 59	125	12.18	2.27	
60 – 69	18	11.89	1.91	
70 and more	4	12.00	4.24	
Total	150	12.13	2.26	

Table (1-3): The mean level of Hs-crp among age group of patients

Sex	N	Mean	Std. Deviation	P- value
Male	92	12.239	2.1502	0.744
Female	58	11.948	2.4382	

Table (1-4): The mean level of Hs-crp among patients' sex

Obese	N	Mean	Std. Deviation	P-value
Obese	21	12.0	2.4	0.889
Non-Obese	127	12.2	2.3	

Table (1-5): Compare the mean levels of Hs-crp according to patients obesity

Hscrp	N	Mean	Std. Deviation	P-value
First time	97	12.247	2.1459	0.52
Second time	48	11.979	2.4537	
Third time	5	11.2	2.7749	

Table (1-6): Compare the mean levels of Hs-crp according to number of CHD attack

Discussion

Inflammation plays an important role in the development of coronary heart disease. Inflammation of coronary arteries is likely an important component of changes in vessel wall morphology. It has been proposed that inflammation of arteries results in an increased production of cytokines, especially interleukin 6, and activation of clotting factors, increased platelet aggregation, and smooth muscle cell proliferation.

The aim of study was to investigate the predictive value of high sensitivity C-reactive protein (hs-CRP) in serum of patients with cardiac diseases and compare with troponin I, and to measure the high Sensitivity C-reactive protein (hs-CRP) in serum of individuals with risks of cardiac diseases and compare with troponin I.

This study showed clear variation in the mean level of hs-CRP with p-value of <0.05 when compared between the control, risk patient and known patient as in table 1-1 and figure 1-1. While the troponin I showed no differences between the control and risk group with p-value of more than 0.05. The results showed that hs-CRP values have predictive evidence before getting attack but the result of troponin showed insignificant changes. These findings were in agreement with the results of James A (13) and Christopher Heesch (14).

In other hand, showed there was clear variation in the mean level of Hs-CRP between the control and risk patients (p-value = 0.000) as shown in table (1-1). But in comparison between risk and control (as shown in table 3-2) for troponin I result showed there was no differences between mean level of risk and control as shown in table (1-2) with insignificant decreased changes with p-value of 0.10. These findings were agreed with Steven E (15) who measured the troponin I levels by ELISA method.

In this is study, the mean value of the hs-CRP according to age individuals we found showed insignificant variations (p-value = 0.885) conflicting with the results of Hala Mahfouz Badran (16) who recommended that the c reactive protein in human above 42 years old is increased slightly. The discrepancy here was due to that all our patients were above 40 years old and also, this study measured hs-CRP while that study measured CRP.

In this is study, the mean value of the hs-CRP according to sex individuals (as in table 1-4) we found that the mean level in male was 12.239 mg/L, where while the mean level in female was 11.948mg/L. This result showed insignificant variation with p-value of 0.744. This is result was disagreed with Ryuichi Kawamoto (17) whose results suggested that hs-CRP levels was greater in women than men.

This inconsistency was due to difference in the study groups between the two studies, as this study was carried out in CHD patients while that study was implemented in healthy individuals.

In this study, the mean value of the hs-CRP when classified according to obesity, the results showed insignificant variations between the obese and non-obese groups (p -value = 0.889) as shown table (1-5). Although this result was agreed with Graziani F (18) but it is dissimilar to Kavita Shalia (19) who explained that the hs-CRP and obesity have strong correlation.

In this study, the mean value of the hs-crp according to number of CHD attack showed insignificant variation with p -value of 0.52 as shown table (1-6). This result was agreed with the report of Louai Razzouk (20).

Conclusion

The amount of the High Sensitivity C-reactive protein (hs-CRP) in serum of patients with cardiac diseases and in serum of individuals with risks of cardiac diseases and compare with troponin I is cleared different .

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