ORIGINAL ARTICLE

Inflammatory Markers as determinant for Acute Coronary Syndrome

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ABSTRACT

The inflammation plays a key role for development and progression of atherosclerosis, therefore acute coronary syndrome (ACS). The study aimed to detection of inflammatory biomarker such as high sensitive C-reactive protein(hs-CRP) and Interleukin-6 (IL-6) concentration in the serum of patients suffering from ACS. The study carried out on 88 subjects were 60 of them were patients and 28 of them were healthy subjects considered as control group , while 60 patients were divided into two groups each group included 30 patients were the first group suffered from myocardial infarction (MI) and the second group suffered from unstable angina pectoris (UAP). Ten milliliters of venous blood were drawn from all subjects to obtain serum and stored at -20 **C**°. The serum used for evaluation of hs-CRP levels by I-ChromCRP reader according to immunofluorescence assay and detection of IL-6 concentration by ELISA . Results of the study revealed the myocardial infarction and unstable angina patients recorded a significant ($p < 0.01$) increase in the concentration of hc-CRP and IL-6 when compared with the control group.So we concluded the inflammatory biomarkers elevated in the serum of patients that reveals the association of hs-CRP and IL-6 with the manifestation of cardiac disease.

Keywords: Acute coronary syndrome, high sensitive c-reactive protein, interleukine-6, myocardial infarction

INTRODUCTION

Acute coronary syndrome (ACS) is one of deleterious disease of the heart that threatens life of the human and considered the chief cause of death worldwide (17 ; 20; 2013). Also considered that ACS ranges from less severe unstable angina to more serious forms, including chronic ischemia to myocardial infarction that leads to sudden heart death[24].

Acute Coronary Syndromes (ACS) which results from acute myocardial ischemia that range from unstable angina to ST-elevation myocardial infarction (STEMI) and non– ST elevation myocardial infarction (NSTEMI). This life-threatening disorder is first cause of emergency medical care and hospitalization[6].

Stable angina occurs when perfusion of coronary artery impaired by stable atheroma in the coronary arteries[11], while unstable angina occurs when a blood clot forms on a plaque, increasing the blockage area and degree in a coronary artery, so the symptoms characterized by pain or pressure that occurs when the blood and oxygen supplied to the cardiac muscle can't keep up with the needs of the myocardium[18]. Many risk factors related with the coronary artery disease that included sex, age, genetic, hyperlipidemia, diabetes mellitus , hypertension and atherosclerosis[3].

Several biomarkers elevate in the serum of patients suffering from ACS such as creatine phosphokinase (CPK), lactate dehydrogenase (LDH), aspartate amino transferase (AST), concentration when there is an inflammation and necrosis of the hepatic tissues, myocardium, and skeletal muscle[14].

Many studies were revealed the association of different biomarkers of inflammation, including acute phase reactants, cellular adhesion molecules, and cytokines with the manifestations of atherosclerotic vascular disease (10). C-reactive protein (CRP) is an acute phase reactant synthesized by the hepatic cells in response to the pro-inflammatory cytokines such as tumor necrosis facto r(TNF) and IL-6[2]. Interleukins particularly IL-6 considered one of the most important key mediator of inflammation[12] and has been implicated in the pathogenesis of atherosclerosis coronary artery disease (CAD)[9].

The positive associations was found between circulating IL-6 level and risk of CAD (5). Mendelian randomization studies indicate that there might exist etiological association between signaling through IL-6R and CAD[7].

MATERIALS AND METHODS

The study carried out on 60 patients suffering from acute coronary syndrome (ACS) that included unstable angina pectoris and myocardial infarction whom were admitted to coronary care unit (CCU) in the General Kirkuk Hospital and Azadi Teaching Hospital in Kirkuk city during 2016 December to 2017 May, while 28 subjects were healthy persons.

Subjects of the study grouped to (3) groups: the first group included 30 myocardial infarction patients were 17 of them male and 13 female their ages range 38 – 81 years old. While the second group included 30 unstable angina patients were 16 male and 14 of them female, were ages range 39 - 78 years. The third group were healthy subjects considered as control group consists of 28 subjects were 15 male and 13 of them female, their ages range from 35 – 70 years.

Ten milliliters of venous blood were drawn from Cubital vein from all subjects and put into clean gel tubes left at the room temperature for 15 minutes for clot formation and then centrifuged for 10 minutes at 3000 round per minute (RPM). Serum was separated and kept in the eppendorf tubes and stored at deep freeze -20 Cº (AL-Hakiem; 2008) then used for detection of IL-6 and hs-CRP concentration.

high sensitive C-reactive protein concentration in the serum were evaluated by the immune-fluorescence assay using

Ichroma™ and hs-CRP reader, according to the kit company product (boditech) informations, while evaluation of IL-6 concentration in the serum were carried out by human IL-6 ELISA kit provided by Diaclone Company (France origin).

Statistical analysis: The results of the study were statistically analyzed by one way analysis of variance (ANOVA), the difference between means were assessed by Duncan test[8].

RESULTS AND DISCUSSION

The results of the study shown in table 1 revealed there was a significant increase (P≤0.01) in the mean level of hS-CRP in the serum of myocardial infarction patients (8.907±0.942)mg/L when compared with the unstable angina patients (5.074±1.094) mg/L and the control group (1.958±0.485) mg/L. Also there was a significant increase (P≤0.01) of the level of hS-CRP in the serum of unstable angina patients when compared with the control group.

Table 1. The mean levels of hs-CRP in serum of myocardial infarction , unstable angina and control groups.

Study groups	No. of subjects	hs-CRP (mg/L) (Mean ± SD)
Myocardial infarction	30	8.907 ± 0.942 a
Unstable angina	30	5.074 ± 1.094 b
Control	28	1.958 ± 0.485 c

a,b,c, :The different letters indicate for the presence of significant difference between groups at the level (P ≤ 0.01).

These results were compatible with the results of (23) that carried out on 90 patients suffering from acute myocardium infarction which showed the rapture of plague recorded a more significant level of hS-CRP (≥3 mg/L) in comparison to the hS-CRP level in the normal healthy group (<3 mg/L).This results suggested that hs-CRP level reflects to the exciting the stability of coronary atherosclerotic plaque that was a reliable biomarker can predict the prognosis of AMI patients, therefore CRP level is a sensitive biomarker of inflammatory activity and its level elevated during inflammatory response (4), so elevation of C-reactive protein (CRP) level has been shown to be useful for predicting the risk of cardiovascular events in patients with determined coronary artery disease (CAD) (10 ; 22).

However CRP also may acts to enhance the release of IL-6 from endothelial cells by activating endothelial production of IL-6 and neutrophils IL-6R shedding at the site of the endothelium (13).

Table 2 shows the results of IL-6 concentration which recorded a significant increase (P ≤ 0.01) in the level of IL-6 in the serum of patients suffering from myocardial infarction (51.03 ± 10.18) pg/ml when compared with unstable angina patients (29.59 ± 6.45) pg/ml and with the control group (14.999 ± 3.261) pg/ml.

Table 2: The mean level of IL-6 in serum of myocardial infarction , unstable angina and control groups.

Study groups	No. of subjects	Conc. of IL-6 (pg/ml Mean ± SD
Myocardial infarction	30	51.03 ± 10.18 a
Unstable angina	30	29.59 ± 6.45 b
Control	28	14.999 ± 3.261 c

A, b, c: The different letters indicate for the presence of significant difference between groups at the level (P ≤ 0.01).

The results of the study also recorded a significant increase (P ≤ 0.01) of IL-6 level in serum of unstable angina patients when compared with the control group. These results compatible with (1; 15) were they observed that the IL-6 is a proximal mediator released under different stimulation, such as IL-1β in different injured or infected tissues. The biomarker IL-6 mainly created by the hepatic cells as a major initiators of the acute-phase reactions[5].

The inflammatory processes are opener factors at the pathogenesis of atherogenesis and acute coronary syndrome[8], so IL-6 considered a pleiotropic pro-inflammatory cytokine and a key mediator of inflammation[21]. This was demonstrated by the elevation of IL-6 levels which was a prognostic feature for the starting of future coronary events in healthy persons as well as mortality in acute coronary syndrome patients[16]. Also IL-6 attributed to the ACS development by affecting to the endothelial, metabolic ,and coagulant events , and also is looked as a local and circulating sign of coronary plaque inflammation[19,25,26].

CONCLUSION

we concluded that the inflammatory biomarkers such as hs-CRP and IL-6 concentration were elevated in the serum of patients suffering from myocardial infarction and unstable angina pectoris.

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