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Combination of Plasma Ultra-Sensitive CRP and Homocysteine as Diagnostic and Predictive Protocol for Acute Myocardial Infarction

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Abstract: ***Objective: The aim of the present study was to provide us-CRP testtogether withhomocysteine test as a protocol for emergency diagnosis for acute myocardial infarction (MI) comparing to cTnI and LDL-C.Materials and Methods: This was a cross-sectional study conducted in Sudan, between December 2012 and July 2014.The study included 122 patients(78 males and 44 females). All the patients were admitted in Intensive Cardiac-Care Unit (ICCU) ward, and informed consent was obtained with the blood samples immediately (within the first 3 hours after chest pain), regardless the type of that disease. Control group was consisted of 80 healthy volunteers.Using enzyme linked immunosorbent (ELISA) methodwe estimated serum homocysteine(Hcy), ultra-sensitivity C – reactive protein (us-CRP), and cardiac troponin I (cTnI); while low-density lipoprotein (LDL-C) is measured by Standard direct automated spectrophotometric method. During the next 24 hours, and as a result of the medical follow-up, the patients were divided into 2 groups, AMI group (68 patients) and non-AMI group (57 patients). Results: The levels of us-CRP in AMI group showed significant increasing (P<0.05) when compared to non-AMI group, as well as comparison with the control group. While Hcy and cTnI displayed a significant increase in AMI when compared to control but showed insignificant raise when compared to non-AMI. On the other hand, the level of LDL-C showed insignificant variations between the three groups.Conclusion:Measurement of CRP together with homocysteine is thus a clinically sensible way to urgent and emergent assess whether a particular patient has acute MI than non-acute MI.***

Keywords: acute myocardial infarction, homocysteine,us-CRP, cTnI,LDL-C

1. Introduction

Despite recent advances in the management of high blood pressure, diabetes mellitus, hyperlipidemia, but still the death due to heart disease is the most common. Acute myocardial infarction (AMI) usually develops to sudden or gradual anterior chest problems. There is a substantial interest in the use of newer biomarkers to identify persons who are at risk for the development of cardiac disease. Measurements of several biomarkers simultaneously will enhance risk stratification in CAD [1].

Diagnosis of acute myocardial infraction is done by the patient's history of illness and physical examination, in addition to cardiac biomarkers (CK-MB, troponins, and myoglobin) and electrocardiogram (ECG) findings. Reliance upon clinical impression alone leads to diagnostic uncertainty because the sign and symptoms of heart failure are relatively nonspecific. Key symptoms such as shortness of breath are nonspecific in patients with comorbidities such as reactive airway disease. Likewise, routine laboratory tests, ECG, and radiographs cannot be relied upon to always guide an accurate and appropriate diagnosis. Despite these challenges, diagnostic capabilities in heart failure have improved in recent years with recognition of the role that many factors play in the disease[2].Now, some newer tests are also being considered to be valuable in the diagnosis of the vascular events. Homocysteine (Hcy) and ultra-sensitivity C – reactive protein (us-CRP) are greater than the product of the individual effects of each risk factor considered alone. Ultra-sensitivity C-reactive protein (us-CRP) and homocysteine have been emerged for diagnosis of coronary artery disease (CAD)[3].Only few cross-sectional and small sized cohort studies have been conducted to explore the association of us-CRP and homocysteine biomarkers in diagnosis of CAD in African population[4].The levels of CRP and HyC must be used with caution in certain populations. Inflammation and some types of lung disease have elevated CRP level without affecting on HyC. While homocysteine is elevated in many other diseases those have no effect on CRP[5]. In 2014Miao et al [5]concluded that the homocysteine concentrations changed little regardless of the form of heart disease but did not change in minor inflammatory cases, whereas CRP concentration considerably increased in inflammations and in acute myocardial infarction (MI). In 2011Bizhe*et al*[6] reported that serum homocysteine concentration was increased in patients with all types of CVD and in acute inflammations.On other hand,on2013Mok*et al*[7]reported that the actual impact of us-CRP and homocysteine needs to be assessed by doing larger prospective studies. Levels of hs-CRP were affected by age, blood pressure and blood glucose while the plasma homocysteine may be an independent risk factor in ischaemic stroke patients.Several epidemiological studies strongly suggest that the CRP with high sensitivity (hs-CRP) can be an independent and valid indicator for heart attack, heart arrest[8]. But, little information available about the combined effect of hs-CRP and homocysteine biomarkers on the risk of Acute MI[4].

The aim of our study was to determine whether the introduction of combined hs-CRP together with homocysteine had an impact on patients presenting with suspected acute MI to the emergency department as a protocol for emergency diagnosis for acute MI comparing to cTnI and LDL-C.

2. Materials and Methods

This study was a cross-sectional study conducted in Khartoum State – Sudan,between December 2012 and July 2014.The study included 122 patients(78 males and 44

females) in mean age of 53.1±7.58 years.All the patients of either sex admitted in Intensive Cardiac-Care Unit(ICCU) wards.Theblood samples were collected from participants at the moment they were hospitalized in ICCU with cardiac disease, regardless the type of that disease. Control group was consisted of 80 healthy volunteers (40 males and 40 females) whose mean ages were matched (48.9±9.14 years).The subjects were nonsmokers, received no drugs and had no metabolic disease and had no recent history of surgery or trauma. Furthermore, the patients with previous history of CVA, malignancy, infection, inflammatory disease,or diabetes mellitus were excluded from the study. To avoid other confounding factors, we excluded overweight patients and controls and/or with a history of folic acid or vitamin B complex supply, a history of folic acid or vitamin B complex deficiency, and renal insufficiency.Informed consent was obtained from all patients and controls, and then pre-prepared questionnaire was used to collect the subjects' data including their past medical history, smoking status, family and clinical histories, and the prescribed drugs.10 ml venous blood samples were taken from in serum separator tubepatients in the first 3 hours after chest pain, while blood samples were collectedafter an overnight (for 10 hours) fasting from the controls group. Serum was separated after 20 minutes and analyzed immediately after separation.The biochemical procedures were done via enzyme linked immunosorbent (ELISA) method. Serum homocysteine was measured using a special kit and ELISA method using AXIS- SHIELD kit (England)[1]. To determine the serum levels of us-CRP, commercial kits of using quantitativeassessment kit from DRG HS ELISA method were used[3]. On the other hand, cardiac troponin I (cTnI) is measured as described byNiebroj-Dobosz*et al*[8], while low-density lipoprotein (LDL-C) is measured by Standard direct automated spectrophotometric method as manufacturer procedure. During the next 24 hours, and as a result of the medical follow-up of patients and after determining the type of cardiac disease, the patients were divided into 2 groups, AMI group (68 patients; 40 males and 28 females) and non-AMI group (57 patients; 35 males and 22 females).

The data obtained are expressed as mean values ± SD. Statistical analyses were performed using SPSS (Statistical Package for Social Sciences).*t*-test was used to test for differences in means of continuous variables between patients and controls.

3. Results

The us-CRP and homocysteine levels in control and AMI groups and the average of their ages are shown in table 1.Levels of us-CRP were raised significantly in both groups of AMI and non-AMI when compared to control group (P=0.00); while the levels of homocysteine, when compared to control group, showed a significant increasing only in AMI group (P=0.00). The level of cTnI also displayed a significant increase only in AMI group when compared to control, but in p value of 0.047 only. LDL-C changed insignificantly between the three groups.

Levels of us-CRP, homocysteine, cTnIand LDL-C were compared between AMI and non-AMI patients in table 2. Levels of us-CRP, homocysteine, and cTnIwere significantly higher in AMI group than non-AMI group (P<0.05). The results of AMI males when compared with the results of AMI females showed significant increasing in cTnI (P=0.044) and insignificant higher levels of both results of us-CRP and homocysteine (P>0.05) as in Table 3.

Table 1: Homocysteine and hs-CRP in controls, AMI and non-AMI patients (mean ± SD)

	Control	AMI	Non-AMI
us-CRP (mg/l)	2.46±2.09	13.77±4.04*	5.32±1.91*
Homocysteine (µ.mol/L)	9.11±2.32	19.46±3.81*	10.15±6.17
Troponin I (ng/ml)	0.45	8.63 *	2.02 *
LDL-C (mmol/L)	94.8±11.1	108 ±7.4	110±8.7

*significant change when compared to control (p value<0.05)

Table 2: Homocysteine and hs-CRP in all cases between patients of AMI and non-AMI patients (mean ± SD)

	AMI	Non-AMI	P value
Number of cases	68	57	
us-CRP	13.77±4.04	5.32±1.91	0.001
Homocysteine (µ.mol/L)	19.46±3.81	10.15±6.17	0.001
Troponin I (µg/L)	8.63	2.02	0.000
LDL-C (mg/dL)	108 ±7.4	110±8.7	0.70

Table 3: Homocysteine and hs-CRP in all patients between males and females

	AMI males	AMI females	P value
Number of cases	40	28	
us-CRP	14.59±5.35	12.95±1.76	0.067
Homocysteine (µ.mol/L)	21.04±2.97	17.88±3.32	0.053
Troponin I (µg/L)	8.98	6.43	0.044
LDL-C (mg/dL)	100.9±10.18	109.6±7.77	0.70

4. Discussion

Many researches used high sensitivity C-reactive protein (hs-CRP)in the diagnosisonsets of cardiovascular disease. Many studies demonstrated that hs-CRP is an independent predictor of future risk for cardiovascular events among healthy persons, as well as among patients with acute coronary syndromes[9].

The present study revealed that levels of serum us-CRP and homocysteine (Hcy) were increased significantly (p-value<0.001) in all patients in ICU when compared to the control group. AMI patients when compared to control group showed significant increase in the levels of us-CRP and Hcy. These results confirmed that plasma Hcylevel was significantly increased in subjects with AMI[10]. Although the non-AMI cases necessitated treatment inside the intensive care unit, but it caused insignificant increase in Hcycomparing to the control. The results of Hcyin this study increased significantly (P=0.001) in AMI patients when compared to non-AMI patients. These findings were in line with Bizhehet al [6] who concluded that the highest Hcyand CRP levels characterized the patients with myocardial infraction.

Also, our findings illustratedthat us-CRP levels were significantly increased in all subjects admitted to ICCU with cardiac problems, but in much higher in patients with AMIcomparing to the control group.Devaraj*et al*[11]concluded that acute coronary syndrome and chronic ischemia are both lead toincreasedserum Hcyconcentration,

and findings of Kawamoto*et al*[12]suggested that mild hyperhomocysteinemiawas associated with multi-vessel coronary artery diseases (CAD) and acute MI. There is growing dispute concerning the causal role of Hcyand more support for the idea that the elevated plasma Hcyconcentration is an aftermath of CAD[13].

The results of the present study elucidated the insignificant increasing in us-CRP and Hcy levels in AMI male patients when compared to AMI female patients (P>0.05).There were some similarities between our results and the results of Sharma*et al*[14]who reported that hs-CRP were affected by age and gender while the plasma homocysteine may be an independent risk factor in ischaemic stroke patients. The level of cTnI was increased significantly (P<0.05) in AMI males when compared to AMI females. These results were agreed with Yiu*et al*[15]who reported that elevation of cTnI in males more than females in healthy persons.On the other hand, LDL-C in AMI males showed insignificant decrease in AMI male patients when compared to AMI female patients (P>0.05).This result was in agreement with that of Swiger*et al*[16]who reported that the concentrations of LDL-C were similar in women and men.

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References

[1] Chan D, Ng LL. Biomarkers in acute myocardial infarction. BMC Medicine 2010,8:34-34.
[2] Braunwald E. The treatment of acute myocardial infarction: the Past, the Present, and the Future. European Heart Journal. Acute Cardiovascular Care 2012,1:9-12.
[3] Wang HE, Shapiro NI, Safford MM, Griffin R, Judd S, Rodgers JB, et al. High-Sensitivity C-Reactive Protein and Risk of Sepsis. PLoS ONE 2013,8:e69232.
[4] Page JH, Ma J, Chiuve SE, Stampfer MJ, Selhub J, Manson JE, et al. Plasma total Cysteine and total Homocysteine and Risk of Myocardial Infarction in Women: A prospective study. American heart journal 2010,159:599-604.
[5] Miao Y, Liao JK. Potential serum biomarkers in the pathophysiological processes of stroke. Expert review of neurotherapeutics 2014,14:173-185.
[6] Bizheh N, Jaafari M. The Effect of a Single Bout Circuit Resistance Exercise on Homocysteine, hs-CRP and Fibrinogen in Sedentary Middle Aged Men. Iranian Journal of Basic Medical Sciences 2011,14:568-573.
[7] Mok CC, Birmingham DJ, Ho LY, Hebert LA, Rovin BH. High sensitivity C-reactive protein, disease activity and cardiovascular risk factors in systemic lupus erythematosus. Arthritis care & research 2013,65:441-447.
[8] Niebroj-Dobosz I, Marchel M, Madej A, Sokolowska B, Hausmanowa-Petrusewicz I. Circulating autoantibodies to troponin I in Emery-Dreifuss muscular dystrophy. Acta Myologica 2008,27:1-6.
[9] Montecucco F, Mach F. New evidences for C-reactive protein (CRP) deposits in the arterial intima as a cardiovascular risk factor. Clinical Interventions in Aging 2008,3:341-349.
[10] Pérez-López FR, Larrad-Mur L, Kallen A, Chedraui P, Taylor HS. Gender Differences in Cardiovascular Disease: Hormonal and Biochemical Influences. Reproductive sciences (Thousand Oaks, Calif.) 2010,17:511-531.
[11] Devaraj S, Singh U, Jialal I. Human C-reactive protein and the metabolic syndrome. Current opinion in lipidology 2009,20:182-189.
[12] Kawamoto R, Tabara Y, Kohara K, Miki T, Kusunoki T, Takayama S, et al. Association between fasting plasma glucose and high-sensitivity C-reactive protein: gender differences in a Japanese community-dwelling population. Cardiovascular Diabetology 2011,10:51-51.
[13] Yakub M, Moti N, Parveen S, Chaudhry B, Azam I, Iqbal MP. Polymorphisms in MTHFR, MS and CBS Genes and Homocysteine Levels in a Pakistani Population. PLoS ONE 2012,7:e33222.
[14] Sharma M, Ganguly NK. Premature Coronary Artery Disease in Indians and its Associated Risk Factors. Vascular Health and Risk Management 2005,1:217-225.
[15] Yiu KH, Lau KK, Zhao CT, Chan YH, Chen Y, Zhen Z, et al. Predictive value of high-sensitivity troponin-I for future adverse cardiovascular outcome in stable patients with type 2 diabetes mellitus. Cardiovasc Diabetol 2014,13:63.
[16] Swiger KJ, Martin SS, Blaha MJ, Toth PP, Nasir K, Michos ED, et al. Narrowing sex differences in lipoprotein cholesterol subclasses following mid-life: the very large database of lipids (VLDL-10B). J Am Heart Assoc 2014,3:e000851.