Relation of Immuno-Inflammatory Markers (IL-6, Crpand ESR Value) With Prediction of Ischemic Heart Disease

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ABSTRACT:

BACK GROUND:

Ischemic heart diseases (I.H.D) become more common during 21st century as the dominant chronic diseases in many parts of the world, and it is predicted to be become the main causes of disability and death world wide. Many factors play a role in pathogenesis of I.H.D among those could be immuno-inflammatory markers which may lead to development of this disease.

OBJECTIVE:

The present study was conducted to obtain more clarification about the impact of some immuno-inflammatory markers (IL-6, CRPand ESR value) on the clinical expression of heart disease among Iraqi patients.

METHODS:

Hundred Iraqi patients with I.H.D (80 male and 20 female) ages ranged from 20 to 80 year were involved in this study, including 4 subgroups: 17 with heart failure (H.F). ; 26 with myocardial infraction (M.I); 12 with stable angina (S.A) and 45 with unstable angina (U.A) who was attending the Iraqi center for heart disease and Baghdad hospital from December 2006 to march 2007. Using enzyme amplified sensitivity immuno assay (EASIA) technique to measure the level of IL-6, and enzyme linked immunosorbant assay (ELISA) technique to measure the levels of CRP, in addition to westergren method to determine ESR were done for both patients groups and healthy control group.

RESULTS:

Significant increased ($p<0.05$) in the serum level of IL-6 in all patients subgroups: MI, HF, UA, and SA. Respectively compared with control group, also all patients subgroups: SA, HF, MI, UA, consequently revealed significant increased ($p<0.05$) in the mean of CRP concentration compared with control group. Moreover, highly significant elevated ($p<0.01$) in the erythrocyte sedimentation rate (ESR) value in the patients subgroups: SA, UA, MI, HF respectively compared with control group.

CONCLUSION:

Elevated levels of inflammatory markers, particularly CRP and IL-6 are a relatively strongly predictor of I.H.D and in one way or another ESR value and CRP level reflect the degree of the inflammatory status of these diseases.

KEY WORDS: ischemic heart diseases, inflammation, IL-6, CRP, ESR.

INTRODUCTION:

Inflammation play an essential role in the development of many diseases, such as types 2 diabetes mellitus, and initiation, progression of atherosclerotic lesion ,and plaque distruption[1,2]. The role of inflammatory mediators and markers has become paramount in understanding and recognizing these, diseases more completely and at earlier stages of pathogenesis [3, 4, 5, 6] .Inflammatory response and cytokines secretion to tissue injury play a particularly active role after MI. [7]Interleukin -6 is an important inflammatory mediator in host defense mechanism and it is the liver [8].

Many authors suggest that elevated CRP levels had a stronger association with cardiovascular risk than low density lipoprotein (LDL) and cholesterol; more over this association was independent of age, smoking, cholesterol, diabetes and hypertension. On the other hand, ESR emerged as a strong predictor of coronary heart disease mortality after 17-23 year after the blood test was performed [13], elevated ESR value indicated a raised cardiovascular risk, even after adjustments for age coronary risk factors [14].

PATIENT AND METHODS:

One Hundred Iraqi patients with I.H.D (80 male and 20 female), including in four subgroups: 17 with H.F; 26 with M.I; 12 with S.A and 45 with U.A) with apparently healthy 20 individuals as control group, the age varied between 20 to 80 years.

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All patients were diagnosed by consultant of heart disease in Iraqi center for Heart Diseases and Baghdad Hospital from December 2006 to March 2007. **Methods:** Serum specimens were assayed by (EASIA) technique to measure the level of IL-6 (Biosource Europe S.A nivelles Belgium)and ELISA technique to determine the level of CRP (Drg ELISA instrument ,GMBH Germany), in addition to estimate erythrocyte sedimentation rate by westergrens method and the value expressed as mm/hr[13].

Statistical analysis: The suitable statistical methods were used in order to analyze and assess the results, by the following.

1- Descriptive statistics

-Statistical tables including observed frequencies with their percentages.

-Summary statistic of the readings distribution (mean, S.D)

2-Inferential statistics

These were used to accept or reject the statistical hypotheses, by the following: Analyses of variance (ANOVA) test

-Least significant difference (LSD) test.(F-test).

-All the statistical analyses were done by using Pentium-4 computer through the spss program (version-10) and excel application [15].

RESULTS:

The concentration of IL-6 level is presented in (table1) ,increased level of IL-6 in all patients subgroups : H.F ,M.I ,S.A and U.A (22.87 ± 18.96),(26.65 ± 23.98),(18.12 ± 11.31) ,(20.471 ± 5.78) respectively which were statistically significant ($p< 0.05$) in comparison with control group (8.50+5.86), and by using L.S.D(F-test) results shows significant difference ($p<0.05$) when compared heart diseases groups with control group. In addition comparison between patients subgroups shows significant difference ($P<0.05$) in IL-6 levels between H.F vs. S.A and M.I vs. S.A and U.A as clearly shown in (table 1).Increases concentration levels of CRP in all I.H.D subgroup: H.F, MI. SA. and UA(71.89± 18.56), (68.49± 20.17) (74.09± 29.72), (62.73 ±16.84) respectively which were statistically significant ($p< 0.05$) as compared with control group (27.90 ± 20.71) , and using L.S.D test appear significant differences when compared I.H.D groups with control group (table2). On the other hand, comparison between patients subgroups shows highly significant difference ($p< o.oo1$) in C-RP level between M.I vs. S.A and H.F, also highly significant difference ($p< 0.001$) among S.A vs. U.A patients groups (table-2). Highly significant increased ($p<0.001$) in E.S.R values in all patients groups: SA, UA, MI, HF (47.00 ±24.81), (46.40±21.80),(43.00±28.17) (38.53±18.13), compared with control group (13.16±12.82).

On contrast statistical comparison between patients group shows non-significant difference as clearly demonstrated in (table 3).

Table 1: Concentration of interleukin – 6 level in patients with ischemic heart disease.

Study Groups	No.	Concentration of IL -6(Pg/ml) Mean ± S.D	ANOVA P.Value	
Control	7	8.50 ± 5.86	0.043	S P< 0.05
H.F	13	22.87 ± 18.96		
M.I	10	26.65 ± 23.98		
S.A	8	18.12 ± 11.31		
U.A	25	20.47 ± 15.78		
Total	63			
Statistical Comparison between study groups L.S.D (F-test)				
Study Groups	P.Value			
Control	H.F	0.021	S.	
	M.I	0.011	S.	
	S.A	0.043	S.	
	U.A	0.044	S.	
H.F	M.I	0.564	N.S	
	S.A	0.047	S.	
	U.A	0.924	N.S	
M.I	S.A	0.027	S.	
	U.A	0.045	S.	
S.A	U.A	0.71	N.S	

S: significant N.S: no significant

Table 2 : Concentration of C - reactive protein level in patient's serum and control group.

Study Groups	No.	Concentration level of C-RP (mg /I.U)	ANOVA	
		Mean ± S.D	P.Value	
Control	14	27.90 ± 20.71	0.013	S P< 0.05
H.F	9	71.89 ± 18.56		
M.I	15	68.49 ± 20.17		
S.A	5	74.09 ± 29.72		
U.A	30	62.73 ± 16.84		
Total	73			
Statistical Comparison between study groups L.S.D (F-test)				
Study Groups	P.Value			
Control	H.F	0.001	H.S	
	M.I	0.833	N.S	
	S.A	0.885	N.S	
	U.A	0.902	N.S	
H.F	M.I	0.001	H.S	
	S.A	0.006	H.S	
	U.A	0.820	N.S	
M.I	S.A	0. 96	N.S	
	U.A	0.733	N.S	
S.A	U.A	0.001	H.S	

S: significant
N.S: no significant

Table3: Concentration of erythrocyte sedimentation rate in patients with ischemic heart disease

Study Groups	No.	Concentration level of E.S.R (mm /h.r)	ANOVA	
		Mean ± S.D	P.Value	
Control	19	13.16 ± 12.82	0.00	H.S P< 0.01
H.F	15	38.53 ± 18.13		
M.I	25	43.43 ± 28.17		
S.A	9	47.00 ± 24.81		
U.A	42	46.40 ± 21.80		
Total	110			
Statistical Comparison between study groups L.S.D (F-test)				
Study Groups	P.Value			
Control	H.F	0.001	H.S	
	M.I	0.00	H.S	
	S.A	0.00	H.S	
	U.A	0.00	N.S	
H.F	M.I	0.536	N.S	
	S.A	0.346	N.S	
	U.A	0.238	N.S	
M.I	S.A	0. 642	N.S	
	U.A	0.542	N.S	
S.A	U.A	0.942	N.S	

S: significant
N.S: no significant

DISCUSSION:

Many studies have mentioned that cytokines are multipotent mediators of inflammation with generalized action in host defense and pathology [16,5]. The events in the inflammatory response are initiated by a complex series of events involving a variety of chemical mediators, whose interaction are still partly understood [18, 5]. The present study shows high serum levels of IL-6 and CRP which associated with increase risk of I.H.D among Iraqi patients, these inflammatory markers are associated with biological and environmental risk factors for cardiovascular events, including components of the

metabolic syndrome (obesity ,insulin resistance diabetes ,hypertension and low HDL-cholesterol levels) and life style factors ,such as smoking, abstinence from alcohol, and physical inactivity[8,9,10]. Furthermore studies denote that increase level of CRP and fibrinogen during the inflammatory process participated in increased risk of cardiac events[18,20].

On the other hand ,CRP is associated with an increased risk of coronary heart disease and the level of this acute phase protein is a significant marker of the risk of CHD even after careful multivariable adjustment [18,19,20]. moreover ,the elevated in the serum levels of IL-6 and CRP have been found in patients with unstable angina and acute myocardial infarction ,but in contrast have not investigated in patients with chronic stable angina (C.S.A) .we hypothesized that decreased IL-6 levels in stable coronary artery disease might be associated with anatomic extention of disease and aspirin administration might reduce cytokine serum levels[12]. The stimulation of cytokines secretion in response to myocardial infarction (M.I) has profound effects on myocardium that provokes at least 4 changes directly in cardiac myocytes that contribute to the phenotype reprogramming or modeling: progressive myocyte apoptosis; myocyte hypertrophy; defects in contractility and inflammatory signal transduction [17, 18, 23].

Chronically, cytokines have additional effects on extra- cellular matrix, integrins, with vascular and cardiac regeneration, and IL-6 is one of the most commonly associated with the remodeling process postmyocadial infarction [5,23].

Furthermore, erythrocyte sedimentation rate was progressively higher in the presence of 1, 2, or 3-vessel disease [24], many authors shows ESR progressively higher in the presence of angiographically documented major narrowing [25,26]. Erythrocyte sedimentation rate is a long – term independent predictor of CHD in both sex, these finding support the evidence of an inflammatory process in atherosclerosis [24]. In addition to positively related between ESR and body mass index, heart rate, serum total cholesterol, and smoking, and inversely related to alcohol consumption [27].

CONCLUSION:

Elevated levels of inflammatory markers, particularly CRP and IL-6 are a relatively strongly predictor of I.H.D and in one way or another ESR value and CRP level reflect the degree of the inflammatory status of these diseases.

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