Production of Inflammatory Markers (IL-8, IL-4and IFN-γ)and risk of Ischemic Hart Diseases

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Summary:

Background: Ischemic heart diseases (I.H.D) become the most common cause of sudden death, and is also the most common reason for death of man and women over 20 years of age in the world. Many Factors Play a role in pathogenesis of I.H.D. among those could be Immune – inflammatory markers which may lead to development of this disease.The present study was conducted to obtain more clarification about the impact of some immuno – inflammatory markers (IL- 8 , IL- 4 and IFN- ∝) on the Clinical expression of heart disease among Iraqi patients .

Patients and methods: Hundred Iraqi patient with I.H.D. (80 male and 20 female) ages ranged between 20 to 80 year were involved in this study, include 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 attending the Iraqi Center for Heart Disease and Baghdad Hospital from December 2006 to march 2007 . For quantitative estimation of serum levels of IL- 8, IL- 4 and IFN- ∝ by Enzyme Amplified Sensitivity Immuno Assay (EASIA) technique for both patients and healthy control groups.

Results: Significant increased (P< 0.05) in the serum level of interleukin – 8 in all patient subgroups: H.F., M.I, S.A and U. A. respectively Compared with control group, also all patient subgroups: H. F., M. I, S.A and U. A. Consequently revealed Significant increased (P< 0.05) in the interleukin – 4 Concentration compared with control group. More over, highly Significant increased (P< 0.01) in the interferon – ∝ concentration in the patients Subgroups: H. F, M. I, S.A and U. A respectively compared with control group.

Conclusion: Elevated level of inflammatory Markers (IL- 8, IL- 4 and IFN – ∝) in all patients of I.H.D reflects the importance immuno – inflammatory elements as risk factor in the pathogenesis of Heart Disease.

Keywords: Ischemic heart disease, Inflammation, IL – 8, IL- 4, IFN – ∝.

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Introduction:

Inflammation has become one of the central themes in the pathogenesis of heart diseases; the role of inflammation mediators and markers has become paramount in understanding and recognizing these diseases more completely and at earlier stager of pathogenesis. Awide range of cardiac disease has been associated with inflammation and cytokines modulation, these included cardiac reperfusion injury, myocarditis and atherosclerosis (1, 2). Inflammatory response and cytokines elaboration are integral components of the response to tissue injury and play a particularly active role during atherosclerosis. The degree of the inflammatory response in turn is an important determinant of the host outcome cytokines are released by the host myocardium to modulate tissue repair and adaptation after injury (3).

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Many studies abroad have mentioned that elevated in the inflammatory cytokines such as interferon – ∝, interleukin – 6 and Interleukin – 8 have been found in patients with unstable angina are related with myocardial cell damage or plague rupture and thrombus formation (3, 4). On the other hand, interleukin -4 is known as apotent anti – inflammatory cytokine, down regulation interferon – ∝ production (5, 6).

Results:

Significant increased (P< 0.05) in serum level of IL-8 in all patients' subgroups: H.F, M.I, S.A and U.A respectively as compared with control group. L. S. D. test revealed significant difference (P<0.05) when compared I.H.D with healthy control group in addition comparison between patients subgroups showed Significant difference (P<0.05) in IL-8 levels between H.F v.s and S.A as clearly show in table – 1

Table – 1 Serum level of interleukin – 8 measured by EASIA in patients with I.H.D and control group

Study Groups	No.	Serum level of IL - 8(Pg/ml)	ANOVA	
		Mean ± S.D	P.Value	
Control	14	27.90±20.71	0.047	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	0.002	H.S	
	M.I	0.009	H.S	
	S.A	0.00	H.S	
	U.A	0.007	H.S	
H.F	M.I	0.919	N.S	
	S.A	0.875	N.S	
	U.A	0.033	S	
M.I	S.A	0.661	N.S	
	U.A	0.783	N.S	
S.A	U.A	0.024	S	

S: Significant
N.S: No significant

Significant elevated (P< 0.05) in IL-4 level in all I.H.D subgroups : H.F, M.I, S.A and U.A consequently in comparison with healthy control group, L. S. D test showed significant differences (P<0.05) when compared I.H.D subgroups with control group , on the other hand , comparison between patients subgroups show significance difference (P< 0.05) in IL-4 levels between H.F v.s S.A and M.I v.s U.A and S.A v.s U.A (table -2) .

Table -2- Serum level of interleukin – 4 measured by EASIA in patients with I.H.D and control group.

Study Groups	No.	Serum level of IL-4 pg/ml	ANOVA	
		Mean ± S.D	P.Value	
Control	6	52.32±25.36	0.028	S P< 0.05
H.F	14	175.92±163.16		
M.I	17	145.18±102.04		
S.A	8	120.52±105.89		
U.A	35	175.25±160.37		
Total	90			
Statistical Comparison between study groups L.S.D (F-test)				
Study Groups	P.Value			
Control	H.F	0.039	S	
	M.I	0.001	H.S	
	S.A	0.031	S	
	U.A	0.042	S	
H.F	M.I	0.821	N.S	
	S.A	0.034	S	
	U.A	0.873	N.S	
M.I	S.A	0. 279	N.S	
	U.A	0.042	S	
S.A	U.A	0.036	S	

S: Significant
N.S: No significant

Highly significant increased (P<0.01) in IFN – ∝ level in all patients subgroups : H.F , M.I , S.A and U.A respectively which were statistically highly significant (P< 0.05) in comparison with control group , and by using L.S.D test appear significant differences when compared I.H.D Subgroups with control group . On contrast statistical comparison between patients subgroups show highly significant differences (P< 0.01) in IFN – ∝ level between H.F v.s U.A ; M.I v.s U.A and S.A v.s U.A also significant difference (P<0.05) among H.F v.s S.A and M.I v.s S.A as clearly demonstrated in (table – 3) .

Table-3- Serum level of interferon – γ measured by EASIA in patients with I.H.D and control group

Study Groups	No.	Serum level of IFN- γ I.U/ml	ANOVA	
		Mean ± S.D	P.Value	
Control	18	1.648±1.378	0.003	H.S P< 0.01
H.F	13	12.02±11.02		
M.I	16	11.04±10.69		
S.A	7	6.26±3.20		
U.A	35	28.67±17.92		
Total	89			
Statistical Comparison between study groups L.S.D (F-test)				
Study Groups	P.Value			
Control	H.F	0.008	H.S	
	M.I	0.006	H.S	
	S.A	0.004	H.S	
	U.A	0.00	H.S	
H.F	M.I	0.567	N.S	
	S.A	0.020	S	
	U.A	0.004	H.S	
M.I	S.A	0. 047	S	
	U.A	0.002	H.S	
S.A	U.A	0.00	H.S	

S: Significant
N.S: No significant

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 compared with apparently healthy 20 individuals as control group , the age varied between 20 to 80 year . All patients were diagnosed by consultant of heart disease in Iraqi Center for Heart Disease and Baghdad Hospital from December 2006 to March 2007.

Methods : Serum specimens for both patients and control group were assayed by (EASIA) technique to measure the level of interleukin – 8, interleukin – 4 and interferon – ∝ (Biosource Europe S.A nivelles Belgium) , and were conducted according to the manufacturing company leaflet .

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

Descriptive statistics:

- Statistical tables including observed frequencies with their percentages.
- Summary statistic of the reading distribution (mean , S. D)

Inferential Statistics:

These were used to accept or reject the statistical hypotheses, by the following.

- Analyses of variance (ANOVA) test.
- Least significant difference (L.S.D) test (F- test).

All the statistical analyses were done by using SPSS program (version – 10) and excel application.

Discussion:

Many studies shows that inflammatory response are initiated by a complex series of events involving a variety of chemical mediator , whose interaction are still partly understood (8,9) . The present study shows high serum levels of interleukin – 8 , interleukin – 4 and interferon – ∝ which associated with increase risk of I.H.D among Iraqi patients , these inflammatory markers are associated with biological and environmental risk factor for cardiovascular events , including components of the metabolic syndrome (obesity , insulin resistance diabetes , hypertension and low high density lipoprotein level) and life style factors , such as smoking , abstinence from alcohol , and physical activity(10,11,12) . Further more studies denote the transient rise in serum interleukin – 8 concentration during the very early phase of acute myocardial infarction , in combination with several recent lines of evidence indicating the importance of injurious activities of neutrophils as a cause of tissue damage in acute myocardial infarction and the potent stimulation of neutrophils by interleukin – 8 , these result strongly suggest that IL-8 is important in development of myocardial injure in acute myocardial infarction (13,14) . On the other hand , interleukin – 8 is released in plasma after acute myocardial infarction and subsequently binds to red blood cell , resulting in only a transient rise of plasma interleukin – 8 and a more prolonged increase of erythrocyte bound IL-8 (13,15). Moreover, the elevated in the inflammatory cytokines such as interferon – ∝, MCP-1 and interleukin – 6 have been found in patients with unstable angina and that are related with myocardial. Cell damage or plaque and thrombus formation (4, 16). Interleukin – 4 is known as a potent anti – inflammatory cytokine , down regulating interferon – ∝ production, some studies found increase levels of (IFN –, IFN- ∝ , IL-4 and IL-10) in both cerebrospinal fluid and plasma samples from patients with multiple sclerosis or a septic meningitis(5,18) . Many authors indicated that some of proinflammatory cytokines have important role in pathogenesis and pathophysiology for myocarditis and cardiomyopathy and found a relation ship between elevated proinflammatory cytokines and the infection by some strains of bacteria such as H pylori and Chlamydia pneumoniae (2, 19).

Conclusion:

Result of present study showed that immuno – inflammatory markers, play a crucial role in the susceptibility of heart diseases this reflected by markedly elevated in the level of IL-8, IL-4 and IFN- ∝ in all patients subgroup of heart disease.

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