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"Serum IL1-beta and biochemical markers in myocardial infarction"

KEYWORDS: Interleukin1-beta, biochemical markers, myocardial infarction

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ABSTRACT

Objective-*To assess serum interleukin-1β concentrations in patients with myocardial infarction and to examine whether serum IL-1β concentrations correlate with biochemical markers.*

Design- *case-control study of patients with myocardial infarction.*

Setting- *Intensive cardiac care unit of major municipal hospital.*

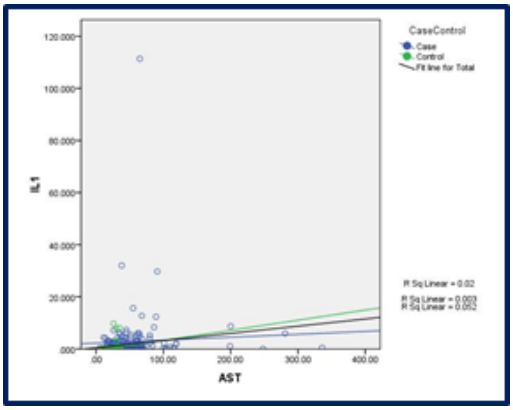
Patients-*patients with acute myocardial infarction*

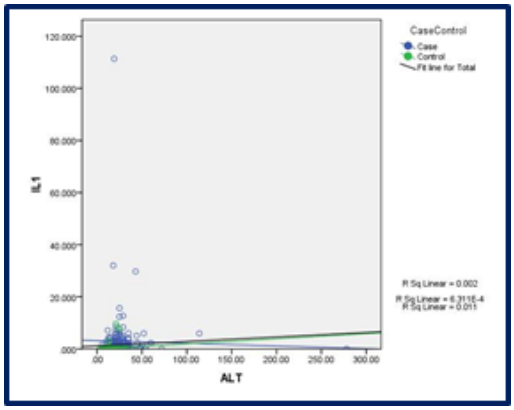
Results-*Mean(SD) serum IL-1β concentrationswere higher (P < 0.001) in patients with MI (n =169; 2.85 (9.34) pg/ml),than in 169 healthy, age-matched controls 0.26 (1.25) pg/ml). Serum IL-1β concentrations had weak positive correlations with TG (r = 0.412, p <0.0005), cholesterol(r =0.196 p <0.0005), AST (r = 0.532, p <0.0005), ALT (r = 0.395, p <0.0005) and ALP (r = 0.314, p <0.0005)*

Conclusion-*Serum IL-1β concentrations are raised in patients with myocardial infarction. The precise role of IL-lβ in coronary artery disease is to be determined.*

Table 1: demographic and clinical characteristics of cases (MI) and controls

		Patients (n= 169)	Controls (n=169)	P value
Age(y) {mean(SD)}		54.73(9.93)	53.98(12.01)	0.607
Sex	Male	132	129	0.697
	Female	37	40	
Smoking		50	5	<0.0005
Alcohol		33	9	<0.0005
Tobacco		70	7	<0.0005
Previous MI		31	0	-
Diabetes mellitus		60	88	0.002
Hypertension		78	80	0.827
Family history	Myocardial infarction	21	0	-
	Diabetes mellitus	30	25	0.461
	Hypertension	2	3	-
	Kidney disease	7	0	-
Height (in cm) {mean(SD)}		163.04(8.06)	161.45(6.38)	0.008
Weight		65.69(9.41)	66.23(8.48)	0.990
BMI		24.74(3.43)	25.40(2.96)	0.040
Serum Triacylglyceride		158.65 (63.36)	95.81 (19.07)	<0.0005
Serum cholesterol		205.81 (57.33)	171.19 (29.37)	<0.0005
Serum AST		55.82 (42.83)	21.99 (7.29)	<0.0005
Serum ALT		27.40 (23.44)	15.60 (6.66)	<0.0005
Serum ALP		226.48 (80.05)	189.29 (24.50)	<0.0005
Interleukin-1β{mean(SD)}		2.85 (9.34)	0.26 (1.25)	<0.0005





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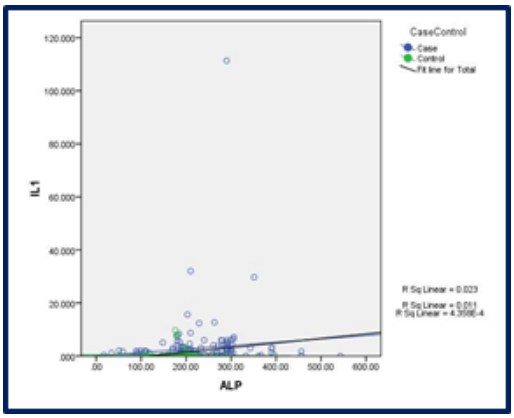

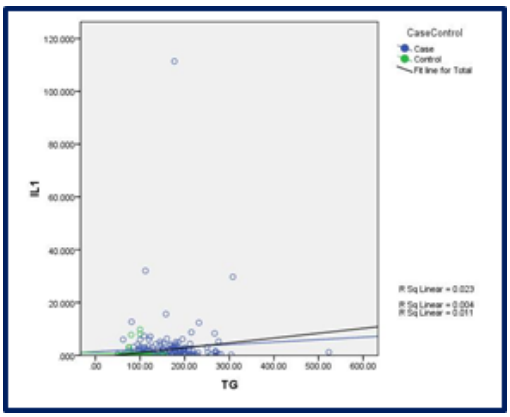

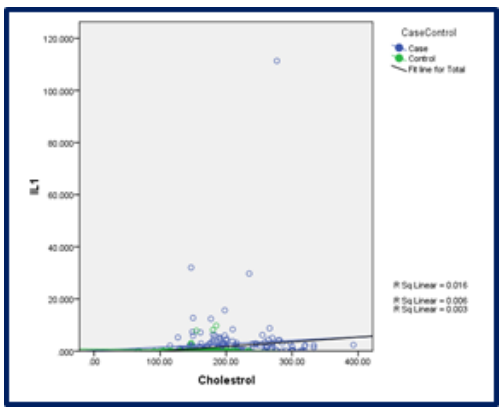

Figure: correlation between serum IL-1β with serum TG, Cholesterol, AST, ALT and ALP. IL-1β is negatively correlated with AST (p= -0.007),

Cytokine is common term for a group of protein cell regulators, differently called lymphokines, monokines, interleukins andinterferons, which are produced by a wide variety of cells in thebody, and play an important role in many physiologicalresponses (1). In the cytokines, Interleukin-1 is a glycoprotein having 17 kDa molecular weight (2). In 1972 Interleukin-1 was first discovered as a lymphocyte-activating factor. Subsequently it was seen that it exerts a variety of effects including induction of inflammation, body temperature increase,stimulation of proliferation of T and B cells, induction ofacute phase proteins and prostaglandins or regulation ofhematopoesis (4).

Both Interleukin-1α and Interleukin-lβ are isoforms of IL-1 and IL-1β is the major circulatory isoforms in humans. Interleukin- 1 is produced by Monocytes, macrophages, and macrophage-derived cellsare the main sources of IL-1 along with the endothelial cells. After stimulation of the cell, IL-1 can effects locally on the surrounding milieu or widespread effects onvarious organs via plasma transport (2).

Currently, in diverse chronic disease inflammation is well established. Interleukin-1 (IL-1), a proinflammatory cytokine with pleiotropic biological effects, appears to be one of the keyplayers of various inflammation-linked disorders. Recently, the role of interleukin-1 in cerebral infarction, rheumatoid arthritis, Alzheimer disease and associated vascular dementia, diabetes mellitus, periodontitis, systemic sclerosis, autoimmune encephalomyelitis is well accepted (4).

In India and all over world cardiovascular diseases (CVDs) are the leading cause ofmortality and morbidity. Coronary artery disease i.e. CHD, is the narrowing of the blood vessels, as a result of atherosclerosis that supply blood and oxygen to the heart which will leads to unstable angina, myocardial infarction(MI) and heart failure. Important contributing factor of inflammation in pathophysiologyof coronary heart disease (CHD), and the inflammatory cascade is particularly important in the atherosclerotic process (3). Important classical risk factor in atherosclerosis includes increased LDL cholesterol level, smoking obesity, diabetes or sedentary lifestyle. But, in the course of time it has come evident that atherosclerosis may also have autoimmune components such as cytokines are likely to participate in pathogenesis of this disorder. Clearly, the recent data shows that atherosclerosis is linked with the activation of the inflammatory processes along with increase of proinflammatory cytokines such as IL-1, IL-6, TNF or C-reactive protein. This in turn causes simple accumulation of lipids into a complex disorder influenced by inflammatory response of arterial wall (4).

Being a pro-inflammatory cytokine, IL-1 plays a major role in atherosclerotic coronary artery disease by various mechanisms. During atherogenesis, IL-1 being a pro-inflammatory cytokine mediate the inflammatory response in the vascular walls. Along with that, IL-1 β had been shown to induce post-cardiac transplantation coronary arteriopathy by augmenting infiltration of inflammatory cells in the vascular walls. It also increases endothelial cell adhesiveness to leukocytes. It induces adhesive molecules which are present on cell surface of vascular endothelium. It also enhances atherogenesis by promoting vascular smooth muscle cell proliferation which increases cell procoagulant activity and acts on lipid metabolism. Moreover IL-1 supresses catecholamine inotropy on heart muscles (2).

Serum cytokine levels are increasingly being used in population studies, yet there are few studies describing the epidemiology of cytokine levels in healthy subjects and in myocardial infarction. this information is important to set the stage for widespread use of Interleukin- 1 level along with cardiac markers in clinical investigations, risk stratification and treatment of the patients. The aim of the study was to assess the role of IL-1 in myocardial infarction and its relation with other biochemical markers. The objectives were (a) to evaluate serum concentration of IL-1β in myocardial infarction. (b) to examine whether IL-1β concentration correlate with serum triacylglyceride, cholesterol, aspartate transaminase, acyl transaminase and alkaline phosphatase.

PATIENTS and METHODS

PATIENTS

The study design was a case control study. This study protocol was approved by institutional ethics committee. Informed consent was taken from all study subjects, both cases and controls after explaining the purpose of the study.

We studied 169 myocardial infarction patients. The cause was presumed to be cardiac with other causes were ruled out after explaining a chest pain in the patients. Patients with chronic illnesses like malignancies, infections, rheumatic arthritis were excluded.

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INTERLEUKIN 1β ASSAY

2DEcho was done after admission of patients complaining chest pain. After that the patient was ruled out for myocardial infarction. Blood was drawn in a plain tube and centrifuged for 10 minutes at 2000rpm. Serum was separated in the screw type vials and stored at -40°C. The serum IL-1β was measured by human IL-1β ELISA ready set go with second generation (Affymetrix, eBiosciences, San Diego, CA, USA). The detection limit was 2pg/ml. 169 healthy age and sex matched controls with no history of any heart diseases and with no any other chronic illnesses like cancer, rheumatic heart disease and the condition in which inflammatory markers would be increased.

Serum triglyceride, cholesterol, AST, ALT and ALP were measured with fully automated biochemistry analyser (AU 400).

STATISTICAL ANALYSIS

Statistical analysis was carried out using SPSS version 16.0 and Microsoft Excel. Descriptive analysis was done for each variable and normality was testes by Shapiro-Wilk test. Bivariate analysis was done using Chi-square test and Mann-Whitney U test. Chi square test was used for nominal variables including past history and family history. For cardinal variables like height, weight, BMI, biochemical markers and inflammatory markers, Mann-Whitney U test was applied. The level of significance was fixed at 0.05. P values <0.05 were regarded as statistically significant.

RESULTS

Table shows demographic variables of patients and controls. There was no significant difference between age (p=0.636) and sex (p=0.295) between patients and controls. For addictions like smoking, tobacco chewing and alcohol intake, there was a significant difference between patients and controls (p≤0.005). No significant difference was seen for BMI in between both the groups. Patients having diabetes has significant difference (p= 0.001) whereas there was no difference in case of hypertension (P=0.572). Family history like diabetes (p=0.702), hypertension (p=0.221) and kidney disease (p=0.006), there was no significant difference among cases and controls.

A significant difference was seen in serum triacylglyceride, cholesterol, AST, ALT, ALP and serum IL-1β as an inflammatory marker (p≤0.0005).

DISCUSSION

MAJOR FINDINGS

In our study we found significantly raised serum concentrations of IL-1β with MI. There was significant correlation between IL-1β as an inflammatory marker with serum TG, cholesterol, AST, ALT and ALP. But the correlation was not very strong. Based on this we suggest that the myocardial infarction which is a major outcome of atherosclerosis may lead to release of serum pro-inflammatory cytokines i.e. IL-1β than in control subjects.

PREVIOUS STUDIES

Ali Ozeren et al. (2003) found the elevated level of increased serum concentration IL-1β and suggested their direct involvement in triggering stage of coronary events, which can be used for determination of high risk unstable angina pectoris (5). D Hasdai et al. (1996) reported the slightly raised serum IL-1β concentration in patients in patients with post infarction accords with its presumed role in response to ischemia and reperfusion. They presumed that, the increased serum IL-1β concentration in their patients with angina might also be result of myocardial infarction (2). Raised serum IL-1β concentration is observed by Wang Y.N. et al (2004) in acute coronary syndrome and stated their significance in diagnosis in acute coronary syndrome (6). Significantly increased in serum total cholesterol and triglyceride was observed by Johny Nijm et al.(2005),studied IL-1,6,10 and 18 but no Il-1β is been studied (7). Ozeren A et al. (1998) studied serum IL-1β along with IL-8 and TNF-α suggesting significant increase in patients with unstable angina pectoris which has major role in development of atherosclerosis with its complications (8). Our study go hand in hand with above studies regarding raised serum IL-1β levels in myocardial infarction with no strongly significant correlation between IL-1β and TG, total cholesterol with strong sample size of 169 case and controls. There is no single study regarding association between serum IL-1 concentration along with the biochemical markers like serum TG, total cholesterol, AST, ALT and ALP in myocardial infarction especially in Indian scenario.

CONCLUSION

Our observation suggests that process of atherosclerosis is the characterized as an inflammation which alters endothelium of coronary arteries. Hopefully, as we have gain more awareness into the role of serum IL-1β in myocardial infarction patients and their significant raised concentrations in MI which can be used for the diagnostic and treatment purpose by the clinicians.

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