



STATUS OF PLASMA INTERLEUKIN-6 AND ITS ASSOCIATION WITH ATHEROGENESIS IN ISCHEMIC HEART DISEASE

Biochemistry

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ABSTRACT

Objective: - The aim of this study was to compare the level of IL-6 in IHD subjects (NSTEMI subjects) with healthy subjects and found the association with atherogenesis. **Methodology:**-The study was conducted on 110 NSTEMI subjects and 110 age and gender matched healthy controls. Plasma IL-6 level were estimated by ELISA technique and Total Cholesterol, serum Triglycerides and HDL-Cholesterol in separated serum sample were estimated by Photometric method on Beckman AU 680 fully automated chemistry analyzer. Difference in all the parameters between NSTEMI subjects and healthy subjects were analyzed by t-test and correlation between two parameters were accessed with Pearson's correlation test. **Results:-** NSTEMI subjects had significantly high levels of Total Cholesterol, Triglycerides and significantly low levels of HDL-Cholesterol was found in NSTEMI when compared with healthy controls. Plasma Interleukin-6 levels were also found significantly high in NSTEMI subjects. A positive significant correlation was observed between Interleukin-6 and Total Cholesterol, Triglycerides and a negative significant correlation with HDL-Cholesterol was found in this analysis. **Conclusion:** - Increased level of IL-6 indicates its role in disease progression. Further, the positive correlation of IL-6 with lipid paradox explains the development of the disease to be related with atherogenesis.

KEYWORDS

NSTEMI, IHD, IL-6

INTRODUCTION

Ischemia is characterized as inappropriate supply of blood to the tissue because of blockage of the blood conveying vessels to the particular regions. It very well might be occur by blood clump or tightening of vein, constantly it is a development of plaque, which is called atherosclerosis.¹ Cardiovascular illnesses caused around 33% passings worldwide² in which Ischemic Coronary illness is generally boundless.³ In 21st century this infection became significant danger factor.⁴ Numerous individuals live with nondestructive Ischemic Coronary illness and weakened personal satisfaction.⁵ Generally 70% of patients have various danger factors for IHD and 2-7% has no danger factors.⁶

The term Inflammation got from latin word 'inflammatio' which means activity of body tissues to risks.⁷ The significant capacity of inflammation is to eliminate the reason for cell injury and fix of tissues. Cytokines are made up by numerous cell bunches yet the transcendent makers are T-cells and macrophages which tie to their particular cell surface receptors and furthermore found in solvent structure.⁸ The primary favorable to inflammatory cytokines have a place with the Interleukin-1 (IL-1), Interleukin-6 (IL-6), Interleukin-17 (IL-17), Interferon and tumor necrosis factor (TNF) families. For the commencement of incendiary course interleukin-1 is important^{9,10} and cytokines have a place with interleukin-6 family have both immunoregulatory and foundational impacts.⁸

The lipid profile is a gathering of tests that are regularly done together to distinguish the danger of Coronary illness. These tests are acceptable pointers of whether somebody is probably going to have a coronary episode or stroke brought about by the blockage of veins or solidifying of the corridors. The lipid profile typically incorporates, significant degrees of Cholesterol in blood flow are firmly connected with movement of Coronary illness. Lipids and lipoproteins have gotten progressively significant in clinical practice, fundamentally on account of their relationship with IHD, in the event of their irregularities known as dyslipidemia, and turned into the significant danger factor for the advancement of this illness, as indicated by epidemiological investigations, particularly in well-to-do nations where fat utilization is high.¹¹

MATERIAL AND METHODS

Subjects

The current examination was led on patients of Ischemic Coronary Disease (NSTEMI) conceded or going to in Department of Cardiology, J.L.N. Medical College, Ajmer. Conclusion of Ischemic Coronary illness was confirmed after assessment of ST section in Electrocardiogram (ECG) by experienced cardiologists. The subjects

remembered for the examination were 110 patients experiencing non ST segment elevated myocardial infarction . 110 healthy control subjects of same age gathering of either gender were chosen for the examination. Consent from every one of the subjects was taken for the investigation. Perplexing variables which could meddle in the biochemical investigation of study subjects and change the outcomes were taking anti hypertensive medications particularly mitigating drugs, subjects with past history of Ischemic Coronary Illness, subjects on oral anticoagulants, subjects with Kidney and Liver illnesses, patients experiencing Diabetes Mellitus, Malignant growth and Thyroid illness, women on chemical substitution treatment, subjects with some other Immune system illnesses and pregnant ladies etc. were excluded from the study.

Measurements

People who were able to get subject of this examination were told about the pre insightful factors. Venous blood sample was taken by aseptic method and gathered in tubes containing Potassium Ethylene Di-amine Tetra Acidic Acid (2% K₂ - EDTA) as anticoagulant for plasma separation and in plain vial for serum separation. Plasma and serum was isolated by centrifugation at 2500 RPM for 10 minutes to obtain clear non-haemolysed serum (Haemolysed serum tests were barred from investigation). Aliquots of tests were set up by moving them into independent plain vials. These were marked appropriately and put away at -20oC until measured. Plasma IL-6 were measured by ELISA technique¹² using Biorad ELISA reader and Total Cholesterol,¹³ serum Triglycerides¹⁴ and HDL-Cholesterol¹⁵ in separated serum sample were estimated by Photometric method on Beckman AU 680 fully automated chemistry analyzer.

DATA ANALYSIS

The results were presented as Mean $\pm$ SD for all quantitative parameters. Differences between means of various parameters were compared by independent t-test. Correlations between variables were tested using the Pearson's correlation test. Statistical analysis was considered to be statistically significant at $p < 0.05$.

RESULTS

Status of various parameters in studied subjects are summarized as follows:-

Table No. 1. Status of various parameters in NSTEMI and Control subjects.

Parameter	Healthy Controls (n = 110)	NSTEMI Subjects (n = 110)	p-value*
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Age (yrs)	57.8 ± 11.9	60.6 ± 12.7	>0.05
SBP (mm/Hg)	116 ± 7.35	139 ± 5.09	<0.0001
DBP (mm/Hg)	82.7 ± 7.79	107 ± 4.29	<0.0001
Pulse rate (Count/minute)	70.4 ± 2.63	71 ± 2.47	>0.05
Total Cholesterol (mg/dl)	133 ± 23	248 ± 24	<0.0001
Triglycerides (mg/dl)	109 ± 17	237 ± 22	<0.0001
HDL-Cholesterol (mg/dl)	51.5 ± 8	28.4 ± 5	<0.0001
IL-6 (pg/ml)	3.7 ± 1.3	8.7 ± 0.6	<0.0001

*p<0.05 was considered as statistically significant.

Table -1 shows significantly (p<0.0001) high levels of Total Cholesterol, Triglycerides and significantly (p<0.0001) low levels of HDL-Cholesterol was found in NSTEMI when compared with healthy controls. Plasma Interleukin-6 levels were also found significantly (p<0.0001) high in NSTEMI subjects [Table 1].

Table 2. Correlation of Plasma IL-6 with Lipid Profile (Total Cholesterol, Triglycerides, HDL-Cholesterol) in NSTEMI subjects.

Parameters	r-value	p-value	Significance*
Total Cholesterol (mg/dl)	0.36	<0.0001	HS
Triglycerides (mg/dl)	0.20	0.036	S
HDL-Cholesterol (mg/dl)	-0.29	0.002	HS

*HS=Highly Significant

As it is shown in table 2, a positive significant correlation (Figure 1 and 2) was observed between Interleukin-6 and Total Cholesterol (0.36), Triglycerides (0.20) and a negative significant correlation (Figure 3) with HDL-Cholesterol (-0.29) was found in this analysis.

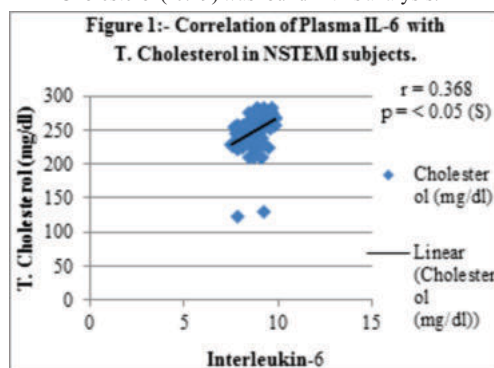


Figure-1. Correlation of IL-6 with total Cholesterol

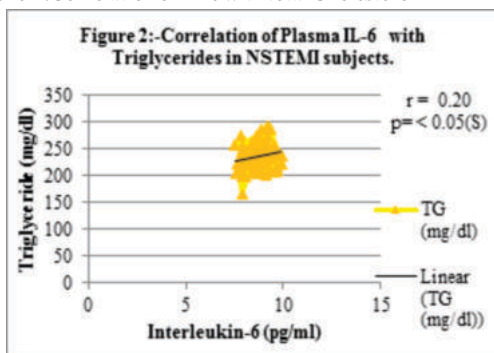


Figure-2. Correlation of IL-6 with Triglycerides

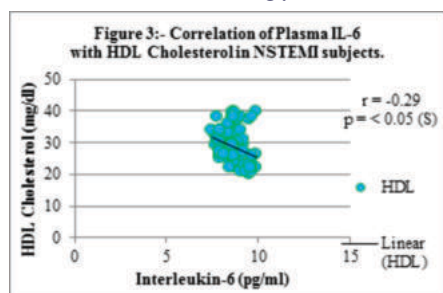


Figure-3. Correlation of IL-6 with HDL- Cholesterol.

DISCUSSION

NSTEMI represents non-ST segment elevated myocardial infarction, which is a sort of coronary failure. Contrasted with the more normal sort of cardiovascular failure known as STEMI, a NSTEMI is regularly less harming to heart. Every heartbeat shows a noticeable waveform on an electrocardiogram (ECG). Although the clinical manifestations of NSTEMIs and STEMI are something similar, their waves look altogether different on an ECG. The two kinds of heart failure are viewed as intense coronary disorders, a term that portrays any blockage of blood supply to the heart muscle. Thus, NSTEMI and STEMI can prompt harm of the heart tissue.

Despite the fact that hypertension is a chief danger factor for cardiovascular end focuses, proof in regards to its position in the assessment of patients with ACS has not given clear-cut results. Apparently hyper-tension may act in a cardioprotective manner at times, for example, the intense period of a MI when hypertensive patients seem to have better in-hospital anticipation.¹⁶ The pathophysiological system of pulse rate related mortality is still subtle. It has been shown that in patients with CAD, elevated pulse rate produces coronary vasoconstriction, possibly further hindering oxygen supply.¹⁷

In the current investigation serum total cholesterol and triglycerides levels were fundamentally higher in NSTEMI subjects in contrast with control subjects. An exceptionally highly significance (p=0.0001) was seen between the groups. Serum HDL levels were lower in NSTEMI subjects when compared with control subjects. A Highly Significant distinction (p=0.0001) in the degrees of serum HDL was also found between the considered gatherings. A study done by Alam MZ et al¹⁸ (2017) reported that dyslipidemia, showed by raised degrees of total and low thickness lipoprotein cholesterol, fatty substances (Total cholesterol, LDL-Cholesterol, TG), low degrees of high thickness lipoprotein cholesterol (HDL-C) is a significant danger factor for CAD. These were the normal lab discoveries among the subjects with STEMI. They tracked down that undeniable degrees of TC (more than 200mg/dl), LDL (in excess of 130 mg/dl), Tg (more than 150 mg/dl) were found in both STEMI and NSTEMI patients which are similar to our study. Low degrees of HDL (under 40 mg/dl) were likewise found in the two kinds of MI. Outcomes additionally uncovered that there was huge contrast of lipid boundary between patients with STEMI and NSTEMI.

A critical positive association of plasma Interleukin-6 with Total cholesterol (p=0.0001), Triglycerides (p=0.036) was found while the relationship with HDL-cholesterol shows a significant negative association (p=0.002) in NSTEMI subjects.

IL-6 may have direct pro- and anti- atherogenic effects on processes associated with development and progression of atherosclerosis. Pro-atherogenic effects include stimulation of vascular smooth muscle proliferation,¹⁹ endothelial cell activation²⁰ and platelet activation²¹ while atheroprotective effects involve lowering of plasma low density lipoprotein (LDL) via upregulated LDL receptor gene expression.²² In human subjects, high IL-6 levels are associated with low HDL, independent of multiple potential confounding variables.²³ Atheroprotective functions of HDL involve transport of cholesterol from the subendothelial intima back to the circulating blood, antithrombotic actions, dampening of inflammation and lowering of oxidative stress.²⁴

So in this analysis, data associating IL-6 with atherosclerotic cardiovascular disease are compelling, but there is also information indicating that this pleiotropic cytokine can act to reduce or resolve inflammation and protect the cardiovascular system.

CONCLUSION

These results suggested the importance of IL-6 in IHD in terms of its clinical manifestations as well as its association with atherogenesis or atheroprotective role. Understanding the mechanism may help to elucidate the pathophysiology of the disease. Since our discoveries depend on a generally low number of vascular occasions, further bigger investigations are expected to affirm these affiliations.

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