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Association of Interleukin-6 with lipid peroxidation and serum lipids in primary hypertension

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Abstract:
Background: *Inflammatory mechanisms play a key role in the pathogenesis of systemic diseases associated with metabolic syndrome or its components such as obesity, insulin resistance, hypertension and atherogenic dyslipidemia. Elevated levels of interleukin-6 (IL-6), a key pro-inflammatory cytokine has been shown to be associated with increased future risk of vascular complications.*
Aim*: The aim of this study was to evaluate the significance of IL-6 levels in hypertensive patients compared with controls and to determine the association of IL-6 with lipid peroxidation marker (malondialdehyde) and serum lipids.*
Materials and methods: *Thirty hypertensive patients with the age group of 30 to 50 years were selected for this study and 30 healthy age and sex matched subjects were selected as control group. Serum IL-6 was assessed by ELISA, malondialdehyde (MDA) was assessed by Thiobarbituric Acid Reactive Substances (TBARS) method and all other investigations were done by ERBA EM-360 fully automated analyzer.*
Results: *The mean levels of serum IL-6 was significantly increased in hypertensive patients compared with controls. Serum IL-6 levels were positively correlated with malondialdehyde, Cholesterol, TGL, LDL and negatively correlated with and HDL.*
Conclusion: *Serum IL-6 might be potentially useful diagnostic marker for the severity of inflammation and also a pathogenic cofactor contributing to chronicity of the disease and vascular complications.*
Keywords: *Interleukin-6(IL-6), Hypertension, Malondialdehyde (MDA)*

I. Introduction

Hypertension is a major risk factor for stroke, myocardial infarction, vascular diseases, and chronic kidney disease .Of the many processes involved in the pathophysiology of hypertension, oxidative stress may lead to functional, structural and mechanical changes in arteries that closely resemble the vascular alterations [1,2] . Vascular changes in hypertension are associated with mechanical and humoral factors that modulate signaling events, resulting in abnormal function, media growth, extracellular matrix deposition and inflammation [3]. Inflammation is a protective response to injury or infection. It is a complex process that involves inflammatory cells first identifying the affected tissue, leukocyte recruitment into tissue, elimination of the offending agent, and repair of the site of injury. Inflammation requires interactions between cell surfaces, extracellular matrix, and proinflammatory mediators [4]. Excessive inflammation can have detrimental effects and contribute to the progression of cardiovascular disease such as atherosclerosis [5]. Interleukin (IL)-6 is a pleiotropic cytokine with a key impact on both immunoregulation and nonimmune events in most cell types and tissues outside the immune system, that is linked to a number of disorders including systemic and pulmonary vascular diseases [6,7]. IL-6 is now considered a major biomarker for cardiovascular risk and the main stimulant for hepatic production of C-reactive protein, a compound widely used as a biomarker for atherosclerosis [8]. MDA, one of the end products of these oxidative reactions, can be detected in several biological fluids and tissues and is therefore used as a biomarker of lipid peroxidation and oxidative stress [9, 10]. Therefore the objective of the present study was to evaluate the significance of IL-6 levels in hypertensive patients compared with controls and to determine the association of IL-6 with malondialdehyde and lipids.

II. Materials And Methods

A total 30 freshly diagnosed hypertensive patients (according to Joint National Committee guidelines) of both sexes aged between 30-50 years attending Department of Medicine, Mamata Medical College, Khammam, Telangana state, India were selected for our study after approval of Institutional Human ethical committee. The anthropological characteristics of patients (age, gender, height, body weight, waist and hip circumferences) were collected. We excluded the patients based on the following criteria: subjects with diabetes mellitus, other

cardiovascular diseases, renal dysfunction, chronic alcoholics, smokers, pregnant women and patients on medication such as antioxidant supplements and lipid lowering drugs. Thirty healthy sex and age matched subjects were selected as controls.

Biochemical analysis:

Fasting blood samples were obtained from the subjects. Samples were centrifuged at 3000×g for 10 min. Samples were analyzed for glucose, lipid profile (Total Cholesterol, HDL, LDL, triglycerides), creatinine using ERBA EM-360 fully automated analyzer. Serum IL-6 was assessed by Enzyme Linked Immuno Sorbent Assay (ELISA).Serum malondialdehyde (MDA) was estimated by Thiobarbituric Acid Reactive Substances (TBARS) method [11].

Statistical analysis: Statistical analyses were carried out with SPSS 20.0. Values were expressed as mean ± standard deviation and mean difference was compared by't' test. p value < 0.05 was considered statistically significant. The Pearson correlation test was used for correlation analysis.

III. Results

Table 1: Comparison of baseline characteristics between controls and Hypertensive subjects.

Parameters	Control group (n=30)	Study group(n=30)	p- value
Age	40.07±5.5	40.6±4.6	0.672
Males (%)	83.3	86.6	NA
Females (%)	16.7	13.4	NA
Body mass index (BMI)	24.0±1.3	26.3±2.9	0.001
Waist/Hip ratio	0.90±0.04	0.92±0.06	0.105
Systolic BP (mm Hg)	114.1±5.8	149.8±7.2	0.001
Diastolic (mm Hg)	73.5±3.2	97.2±5.0	0.001

Data are expressed as mean ±SD, p value <0.05 was considered statistically significant.

Table 2: Comparison of biochemical parameters between control and Hypertensive subjects.

Parameters	Control group (n=30)	Study group(n=30)	p- value
Fasting plasma glucose (mg/dl)	82.7±9.5	84.8±10.6	0.422
Serum cholesterol (mg/dl)	164.5±17.1	193.1±27.6	0.001
Serum Triglycerides (mg/dl)	93.5±25.3	139.3±39.7	0.001
HDL cholesterol (mg/dl)	42.5±5.4	39.2±4.1	0.009
LDL cholesterol (mg/dl)	112.1±19.5	127.3±21.4	0.005
Creatinine(mg/dl)	0.69±0.14	0.8±0.19	0.013
Malondialdehyde (µ mol/L)	1.8±0.32	2.8±0.51	0.001
Interleukin-6 (pg/ml)	0.84±0.22	2.13±0.71	0.001

Data are expressed as mean ±SD, p value <0.05 was considered statistically significant.

Table 3: **Correlation between Serum IL-6 &measured parameters**

Parameters	Correlation Coefficient(r)	p- value
Malondialdehyde	0.569**	0.001
Cholesterol	0.515**	0.002
TGL	0.639**	0.001
HDL	-0.578**	0.001
LDL	0.369**	0.004
BMI	0.380**	0.003
Waist /Hip ratio	0.081	0.539
Systolic BP	0.695**	0.001
Diastolic BP	0.623**	0.001

**Correlation is significant at the 0.01 level (2-tailed).

IV. Discussion

Hypertension is the commonest risk factor for cardiovascular disease and it is also a component of the metabolic syndrome, which is defined as the combination of obesity, insulin resistance, glucose intolerance, and hyperlipidemia [12].Serum IL-6, malondialdehyde and lipid levels were assessed in hypertensive patients and healthy volunteers. This study was undertaken to find out the association of IL-6 with lipid peroxidation biomarker malondialdehyde and lipids.

In the present study, we observed that IL-6 levels were significantly increased in hypertensive subjects. It also correlated positively with systolic and diastolic blood pressure, which is indicating its relevance of low grade systemic inflammation. Interleukin (IL)-6 is a pleiotropic cytokine with a broad range of humoral and

cellular immune effects relating to inflammation, host defense, and tissue injury, produced in response to several factors, including infection, IL-1, interferon-γ, and tumor necrosis factor [13,14]. Elevated levels of IL-6 have been observed in several autoimmune disorders, arthritis, Castleman syndrome, psoriasis, mesangial proliferative glomerulonephritis, and inflammatory bowel diseases [21].However, experimental studies indicate that vascular endothelial and smooth muscle cells from normal and aneurysmal arteries produce IL-6 [15,16,17]. IL-6 gene transcripts are expressed in human atherosclerotic lesions and IL-6 may have pro coagulant effects [18, 19].

In addition IL-6 levels show strong positive correlation between malondialdehyde, BMI, total cholesterol, LDL, TGL and negative correlation with HDL. In this regard, the current data support the hypothesis that, chronicity of hypertension may lead to inflammation.

Oxidative stress can be described as a condition resulting from an uncontrolled increase in free oxygen radicals or an insufficiency in the antioxidant system under certain pathological states. Free oxygen radicals have important toxic effects; chiefly the hydroxyl radical and to a lesser extent the superoxide anion lead to peroxidation of membrane lipids thereby causing production of MDA [20].

Serum IL-6 might be a potentially useful diagnostic marker for the severity of inflammation and also a pathogenic cofactor contributing to chronicity of the disease and vascular complications.

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