

Original article:

High sensitive C- reactive protein and ceruloplasmin in hypertension

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Abstract:

Background: Essential hypertension is the most prevalent form of hypertension accounting for 90% of all cases of hypertension (HTN). HTN is prevalent all over the world. Usually it is readily detectable, easily treatable condition and if left untreated may lead to serious complications. It ranked third in the world by prevalence. HTN double the risk of cardiovascular diseases (CVD), including coronary heart disease (CHD), congestive heart failure (CHF), ischemic and hemorrhagic stroke, renal failure and peripheral arterial disease. The present study was planned to measure the serum levels of high sensitivity C-reactive protein (hs-CRP) and ceruloplasmin (Cp) in patients with essential hypertension (EHT) and to compare with controls.

Material and methods: In this study total 90 subjects were included above 40-65 years of age. These patients were newly diagnosed by clinicians and blood sample were collected before starting antihypertensive treatment and 30 subjects were recruited as controls. hs-CRP and ceruloplasmin levels were measured by the methods of latex turbidometric method and turbidometric immune assay method respectively. Data were analyzed using 'F' test for their level of significance.

Results: The mean hs-CRP and ceruloplasmin level were significantly higher in patients as compared to the control subjects. The significant correlation was observed between the levels of hs-CRP & Cp in essential hypertensive patients.

Conclusions: Elevated serum hs-CRP and ceruloplasmin level might contribute to the increased susceptibility for the development of CVD in essential hypertensive patients.

Key words: essential hypertensive patients, hs-CRP and ceruloplasmin

Introduction:

HTN is major health problem in developed as well as developing countries with a common end result of elevated B.P. Essential HTN refers to the high blood pressure (HBP) with no identifiable cause. ^[1]HTN is the 3rd leading killer in the world and is responsible for 1 in every 8 deaths. About 1 billion people are affected by HTN worldwide. ^[2] In India, death from coronary heart disease rose from 1.17 million in 1990, 1.59 million in 2000 and was expected to rise to 2.03 million in 2010. ^[3] Pooling of epidemiological data showed that HTN was present in at least 25% of the urban and 10% rural adult population in India. ^[4] Thus, HTN is one of the

commonest ailments afflicting our society. Although the exact burden in the Indian Scenario is not known, several small studies point towards its being endemic specially in the urban population. The disease has slow smoldering cause but high morbidity and mortality not adequately controlled. ^[5]

Several mechanisms are implicated in pathogenesis of EHT. These are inflammation, endothelial cell dysfunction and oxidative stress and latter has been intimately related to thrombogenesis and atherogenesis. ^[6] Better understanding of these mechanisms can help proper preventive and measurement strategies for HTN patients. Hence we planned to estimate biochemical

parameters relevant to the process of inflammation and oxidative stress. Assay of CRP allows for accurate measurement of CRP within the previously quantified normal range using traditional assay for CRP. (7) So we decided to measure hs-CRP in EHT patients. We also planned to estimate ceruloplasmin, acute phase protein as well as antioxidant.

Material and methods:

The present study was carried out in the Department of Biochemistry, Government Medical College, Miraj and

study protocol was approved by institutional ethics committee, Study group included 90 patients 40-65 years of age These patients were newly diagnosed by clinicians on the basis of clinical examination and persistent high blood pressure confirmed by 3 separate sphygmomanometer measurements of blood pressure.

The newly diagnosed EHT patients were classified into 3 categories of HTN according to JNC VI(8) as follows.

JNC VI category of HTN	SBP mmHg	DBP mmHg
Stage I	140-159	90-99
Stage II	100-129	100-109
Stage III	>180	>110

Control group included 30 subjects without hypertension (SBP 120-129 mmHg, DBP 80-84 mmHg) and matching in age and sex patients.

Exclusion criteria:

The subjects having other diseases like tuberculosis, diabetes mellitus, malignancy, stroke, auto immune disease, hepatic and renal diseases were excluded from the study. Biochemical parameters were determined before starting antihypertensive treatment. For this blood samples

(were collected taking all aseptic precautions. After separation of sera hs-CRP was determined on fresh sample and stored sera (0-4^{0C}) were used for estimation of ceruloplasmin. Estimation of hs-CRP was carried by Latex-turbidimetric method(9) and estimation of serum ceruloplasmin was performed by turbidometric immuno assay(10). The statistical analysis was performed using Minitab software. The data of patients and controls was analyzed by 'F' test.

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Table No. 1 Serum (hs-CRP) and Ceruloplasmin levels in essential hypertensive patients and controls.

Subjects	hs-CRP mg/L Mean±SD	Ceruloplasmin mg/dL Mean±SD
Stage I essential hypertensive patients (n=22)	3.89±0.50*	75.16±9.17*
Stage II essential hypertensive patients (n=36)	5.78±0.50*	116.7±8.25*
Stage III essential hypertensive patients (n=32)	9.71±1.47*	167.75±11.76*
Controls (n=30)	2.11±0.55	34.60±6.17

(The statistical method used to compare data was “F” test, *P < 0.001 highly significant.

Discussion:

We observed that, the levels of pro-inflammatory marker hs-CRP is significantly increased in EHT patients as compared to that of healthy controls. Sesso HD etal (1999)^[11], Pearson TA^[12] etal have shown that CRP levels are associated with future development of HTN, which suggests that, HTN is in part an inflammatory disorder. HTN may cause increase in pulsatile load and cyclic wall stress on the vasculature, which in turn may affect endothelial cell gene expression of cytokines and ultimately this may leads to increase in inflammatory markers.^[13] Our results show an association between hs-CRP level and severity of HTN. Thus, management of hs-CRP which is

considered as the most robust and prototypic downstream marker of inflammation can be the strongest correlation factor for future clinical events due to vascular inflammation in the newly diagnosed HTN patients.^[7] Among the three group of HTN patients hs-CRP level was found to increase significantly and stagewise. This finding demonstrates a correlation between hs-CRP concentration and severity of HTN.

The mean ceruloplasmin level of EHT patients showed significantly (P<0.001) and stagewise increase as compared to healthy controls.(Table No.1 P<0.001) Kedziora K. K. Bartoz G. etal (2006) also support our study.^[14] Ceruloplasmin acts as an important

extracellular antioxidant through ferroxidase activity. Ceruloplasmin converts toxic Fe^{2+} to Fe^{3+} . Antioxidants play an important role in preventing free radical damage. Increased ceruloplasmin levels observed by us may be associated with generation of oxidation products i. e. O_2^- and H_2O_2 with concomitant production of H_2O from H_2O_2 and ceruloplasmin acting as acute phase reactants.^[15]

Correlation between hs-CRP and ceruloplasmin levels:- Positive and highly significant correlation was observed between levels of hs-CRP and ceruloplasmin in stage I, II & III of essential hypert-

ensive patients (graph No.1)Hs-CRP and ceruloplasmin both are synthesized in liver, these are systemic nonspecific inflammatory markers, whose plasma conc. Increase in response to inflammation. Correlation between conc. of the two positive acute phase proteins suggest that inflammation participate in the development and pathogenesis of inflammation and HTN may be considered as a low grade inflammatory disease. This assay can be used in the prediction of CV risk and for selection of the drug for the management of HTN.

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