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INFLAMMATORY MARKERS HIGH SENSITIVITY C - REACTIVE PROTEIN AND SIALIC ACID IN HYPERTENSION

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ABSTRACT Acute-phase reactants protein whose concentrations in blood increase/decrease by 25% during inflammation. The synthesis and degradation of sialic acid are distributed in different compartments of the cell and inflammation plays a major role in measurement of inflammatory markers such as high-sensitivity C-reactive protein (hsCRP) may provide a method for detecting individuals at high risk of plaque rupture. CRP has emerged as one of the most important inflammatory marker. Objective: The study was to findout the levels of hsCRP and sialic acid in hypertensive subjectss. Methods: The study included 120 volunteers, who were divided into 40 controls, and 80 hypertensive subjects, between the age group of 30-55 years. hs-CRP, total sialic acid, fasting blood sugar, body mass index and lipid profile were estimated in both groups. Past history of CHD, secondary hypertension and metabolic disorders were excluded. Results: Sialic acid and hs- CRP levels were significantly elevated in the hypertensive group than control group. There was significant correlation between hs-CRP and total sialic acid with systolic and diastolic blood pressure. Conclusion: Our result concluded that higher hsCRP levels are significantly correlated with hypertension subjects; there is an association between serum sialic acid and hs-CRP levels. hs-CRP and total sialic acid were positively correlated with dyslipidemia thus contributing to cardiovascular risk.

KEYWORDS : Malondialdehyde (MDA), high sensitivity C reactive protein (hsCRP), Sialic acid

Introduction:

Hypertension is an worldwide public-health challenge because of its concomitant risks of cardiovascular and kidney disease.[1,2] In terms of attributable deaths, raised blood pressure is one of the leading physiological risk factor to which 13% of global deaths are attributed.[3] Elevated hsCRP concentrations have also been associated with endothelial dysfunction, differentiation of macrophages, and smooth muscle cell proliferation.[4] Lifestyle factors that increase the risk include high intake of salt, excess body weight, smoking, family history and alcohol.[5][6] Lifestyle changes and medications can lower blood pressure and decrease the risk of health complications.[7] hsCRP has been shown to correlate with endothelial dysfunction and relate to the Revelo-angiotensin system (RAS), suggesting that hypertension may be in part an inflammatory disorder.[8] Since the association of inflammatory markers and hypertension is not very clear. Studies have explored interrelationship between levels of hsCRP and hypertensive risk factors, and data from these reports have been improper.[9, 10, 11, 12] There is a loss of balance between oxidative stress and antioxidant status is seen in hypertension. This leads to tissue damage through lipid peroxidation anion free radicals [13] The present study is aimed to evaluate the concentration of sialic acid and high-sensitivity C-reactive protein in hypertensive subjects and compare the results with healthy controls.

SIALIC ACID:

Sialic acids comprise of N-acyl derivatives of 9-carbon sugar neuraminic acid. Sialic acids are terminal sugar components of the oligosaccharide chains of glycoproteins and glycolipids. In human beings it is present in body fluids like blood serum.[14] 80% of sialic acids in human serum is N-acetylneuraminic acid and approximately 20% is Neu5Ac 9 Lt.[15] Human serum sialic acid has been correlated with lipids [16,17] Crook et reports that sialic acid was found to be higher in groups with high serum triglycerides or cholesterol and significantly lower in a group with high HDL cholesterol. [18] Serum sialic acid is considered as a marker of innate immunity and activated innate immunity is a risk factors for cardiovascular disease mortality in type 2 diabetes.[19] Most recently study says, in a 17 year-follow up study serum sialic acid has been proposed to be a long – term predictor of CHD events in adults, especially in womens.[20]

Figure 1: Described effects from Silaic Acid

CRP (C-reactive protein)

C-reactive protein is an annular pentameric protein which is found in blood plasma, whose levels rise in response to inflammation. It is an acute-phase protein of hepatic origin that increases following interleukin-6 secretion by macrophages and T-cells [21] CRP is synthesized by the liver It is a member of the pentraxin family of proteins. CRP is mainly used as a marker of inflammation. Apart from liver failure, there are few known factors that interfere with CRP production.[22] Interferon alpha inhibits CRP production from liver cells which may explain the relatively low levels of CRP found during viral infections compared to bacterial infections.[23]

Levels of hsCRP [24]

Low: hs-CRP level under 1.0 mg/L
Average: between 1.0 and 3.0 mg/L
High: above 3.0 mg/L

CRP is a more sensitive and accurate reflection of the acute phase response than the ESR.[25]

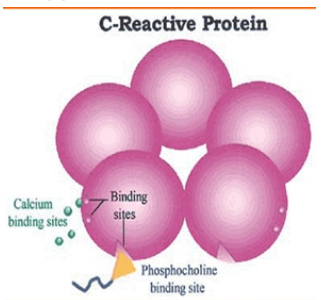

Figure 2: CRP binding capacity of Pentameric Structure

Materials and methods:

This study was carried out in the Department of Biochemistry, Rajah Muthiah Medical College and Hospital, Annamalai University. A volume of 5 ml of fasting venous blood sample was collected in Clot activator tube with aseptic precautions and serum were separated, aliquoted and kept at -20ºC for testing. 120 subjects of both male and female age group between 35 – 55 years were included in the study. 80 subjects were hypertension with blood pressure of 140/90mmHg and 40 subjects were considered as healthy subjects with normal blood pressure of 120/80mmHg. Patients with secondary hypertension, past history of stroke, coronary artery disease (CAD), myocardial infarction, and peripheral vascular disease and diabetes mellitus and those on metabolic diseases was excluded from the study. Serum lipid profile, plasma total antioxidant status (TAS) and serum thiobarbituric acid reactive substances (STBARS) hsCRP and sialic acid were estimated by standard procedures and the values were compared with healthy control subjects. Total cholesterol, high density lipoprotein cholesterol (HDL-C), Triglyceride (TG), was estimated using Erba assay kits. Low density lipoprotein cholesterol (LDL-C) was calculated by Freidewalds formula.

Result:

Sialic acid and hs- CRP levels were significantly elevated in the hypertensive group than control group. There was significant correlation between hs-CRP and sialic acid with systolic and diastolic blood pressure. Compared values between the study groups shown in table 1 and correlation between the blood pressure and inflammatory markers shown in table 2. There was a significant relationship between the study groups.

Statistical software:

Statistical software was used to analyze data. Microsoft word and excel have been used to generate table. Student t test, Chi-square and Fischer exact test has been used to find the significance of various parameters among cases and controls. Data presented are mean ± SD. Analysis of data was done by student t test. A p value < 0.05 was considered significant.

Table 1: Comparison of study variables in test and control groups

Variables	Test group	Control group	P value
FBS (mg/dl)	91.30±9.22	86.66±5.83	0.002
BMI	25.2±0.3	24.3±0.4	0.17
SBP(mmHg)	158.15±10.46	121.39±8.03	0.001
DBP(mmHg)	102.15±6.16	81.08±4.70	0.001
Triglycerides (mg/dl)	126.97±29.29	111.78±23.91	0.002
Total cholesterol (mg/dl)	189.71±25.99	175.95±23.42	0.002
HDL(mg/dl)	43.73±2.79	54.34±4.72	0.004
LDL (mg/dl)	89.28±19.90	81.83±13.51	0.022
hsCRP	3.86±1.04	3.42±0.63	0.008
Sialic acid	3.53±1.17	2.72±0.71	0.0001

Table2: Correlation between inflammatory markers and BP

PARAMETERS	r- Value	p- value
Systolic BP vs SA	0.24	0.004
Diastolic BP vs SA	0.45	0.001
Systolic BP vs hsCRP	0.73	0.001
Diastolic BP vs hsCRP	0.32	0.001
Sialic Acid vs hsCRP	0.70	0.003

Discussion:

The amount of sialic acid released enzymatically and it is correlated with the total sialic acid residues on the surface of the erythrocyte.[26] Serum sialic acid estimation, however, in different racial groups may be useful to assess individual at risk of cardiovascular diseases.[27] Reduced sialic acid content and electrophoretic mobility of erythrocytes has been observed in patients with AMI[28, 29, 30]. It has been suggested that increased plasma sialidase activity in patients with AMI may be associated with clumps of erythrocytes that may alter flow in the microcirculation.[31] Blood pressure values occur within a continue and are determined by hormonal and environmental factors. This inflammation indicates associated with hypertension. Ki Chul Sung et.al, found that hsCRP is to be an independent risk factor for development of hypertension in Korean population.[32] This association between higher hsCRP and new-onset hypertension led Sesso et al to suggest that hypertension is an inflammatory disease.8 Identifying the risk factors for early hypertension would be of great significance in preventing cardiovascular disease [33]. Virdis A et.al denotes experimental data from cross-sectional studies in humans indicate a relationship between hsCRP levels and blood pressure [34]. In particular, hsCRP is related with markers of arterial stiffness, thus suggesting a specific interaction between hsCRP and systolic blood pressure.[35] There is probably a link between dyslipidemia in hypertensive patients and impaired antioxidant efficiacy. Hypertensive patients with abnormal lipids profile, have reduced protection from antioxidants, which may contribute to the predisposition for the development of various cardiovascular diseases [36] We have shown that abnormal lipids profile, specified as high levels of LDL-C and TG and low levels of HDL-C together with low levels of TAS have important value in hypertensive patients.[37] Hypertension frequently coexists with obesity, diabetes, hyperlipidemia, or the metabolic syndrome; their association with cardiovascular disease has been well established.[38] hsCRP can damage vascular endothelial cells, reduce the release of nitric oxide and prostaglandin, and weaken the vasodilatation function; (2) Elevation of blood pressure can damage vascular endothelial cells and activate the inflammation response, followed by elevated hsCRP.[39,40]

Conclusion:

Our result concluded that higher hsCRP and sialic acid levels are significantly correlated with hypertension; there is an association between serum sialic acid and hs-CRP levels. Both inflammatory markers were positively correlated with dyslipidemia thus contributing to cause cardiovascular risk in future. Inflammation may be the bridge which connects atherosclerotic effects of hypertension to future CVD complications.

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