Evaluation Of High Sensitivity C - Reactive Protein and Serum Lipid Profile In Prehypertension and Essential Hypertension

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Abstracts: **Background:** Hypertension is a common, asymptomatic, readily detectable disease that leads to lethal complications if left untreated. Vascular inflammation may be involved in both the initiation and development of hypertension that is evident from the elevated levels of inflammatory markers like Tumor necrosis factor-α, Interleukin-6 and C-reactive protein (CRP) found in people with hypertension with no evidence of cardiovascular disease. hsCRP is associated with an increased risk of incident hypertension at all baseline blood pressures and among individuals without traditional coronary heart disease risk factors. **Objectives**: The present cross-sectional study was an attempt to evaluate the relationship of serum hsCRP levels and serum Lipid profile in prehypertensives and hypertensive. **Material & methods**: The study group included thirty diagnosed cases of prehypertension and hypertension each, attending medicine OPD at a tertiary care hospital. A healthy group of normotensive volunteers were taken as controls. Fasting blood samples were collected for measurement of serum lipid profile and hsCRP (by CLIA).**Results:** There was statistically significant rise in hsCRP levels in hypertensives as compared to controls and normotensives ($p<0.001$). The concentration of cholesterol, triglycerides and LDL-C were significantly high in hypertensives as compared with normotensives ($p<0.001$). **Conclusion:** Findings of higher levels of hsCRP in hypertension along with atherogenic lipid profile suggests that elevated hsCRP and hypertension can be independent determinants of cardiovascular risk. [Dawari S NJIRM 2014; 5(1) :1-5]

Key Words: Hypertension, hsCRP, Lipid profile

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Introduction: A Hypertension is a commonly occurring, readily detectable disease. It is most often is asymptomatic in nature that leads to lethal complications if left untreated.[1] Approximately 7.6 million deaths (13–15% of the total) and 92 million disability-adjusted life years worldwide were attributable to high blood pressure in 2001. It is an established risk factor for development of atherosclerosis and various cardiovascular diseases (CVDs) like coronary heart disease (CHD), renal failure, congestive heart failure (CHF), ischemic and hemorrhagic stroke and peripheral vascular disease.[2]

Recent evidence indicates that vascular inflammation may be involved in both the initiation and development of hypertension.[3] This is evident from the elevated levels of inflammatory markers like Tumor necrosis factor-α (TNF-α), Interleukin-6 (IL-6) and C-reactive protein (CRP) found in people with hypertension with no evidence of cardiovascular disease.[4]

Endothelial dysfunction along with low grade inflammation were associated with greater arterial stiffness in a prospective study.[5]In the year 2001, a cross-sectional study conducted by Bautista et al, for the first time measured CRP in hypertension and found CRP to be an independent risk factor for the development of hypertension.[6] Therefore we designed the study to evaluate the relationship of serum high sensitive C-reactive protein (hs CRP) and lipid profile levels in prehypertensives and hypertensives.

Material and Methods: Present study was a non randomised cross sectional study conducted in department of biochemistry of our college between January2012 to December 2012; after obtaining approval from institutional ethical committee.

The study was conducted on patients attending medicine OPD at University medical college with a tertiary care hospital. The study group comprised of One hundred twenty (120) participants. They were divided into three groups according to JNC-7 classification:[7]

Group A- Normotensive Control: comprised of thirty (30) age and sex-matched normotensives i.e. those with blood pressure <120/80mmHg.
Group B- Prehypertensive: comprised of thirty (30) prehypertensives with blood pressure in the range of 120-139/80-89mmHg
Group C- Hypertensives: comprised of sixty (60) patients including: known cases of essential hypertension, newly diagnosed cases of essential hypertension which included patients with Stage-I [140-159/90-99 mmHg], Stage-II [>160/>100mmHg] and those on anti-hypertensive treatment.

Exclusion criteria: Smokers and alcoholics, Pregnant women, participants suffering from Diabetesmellitus, Endocrine pathologies, Recent illness, previous history of Ischemic Heart Disease /Myocardial Infarction / stroke Peripheral vascular disease and other vasculitis Chronic inflammatory diseases like Systemic Lupus Erythromatosis/ Rheumatoid Arthritis / Osteoarthritis Malignancies Renal and hepatic disorders as well as participants on Medications like steroids, statins, anti-inflammatory drugs were excluded from the study.
After an overnight fast of 12-14hrs,2 ml of fasting blood sample was collected by venous puncture with all aseptic precautions in a plain vacutainer. Blood was allowed to clot. Serum was separated by centrifugation at 2500 rpm for 5 minutes at room temperature and was free from hemolysis and turbidity. The serum was subjected for estimation of High sensitive C-reactive protein (hs-CRP) by Chemiluminescence Immunoassay (CLIA)[8] using automated CLIA system. Estimation of serum lipid profile was done by using automated biochemistry analyzer. The methods used were as follows: Serum Total Cholesterol (CHO) by Cholesterol oxidase-peroxidase (CHOD-PAP) method [9], Serum Triglycerides (TG) by Glycerol phosphate oxidase method, Serum High Density Lipoprotein Cholesterol (HDL) –direct enzymatic method, Serum Low Density Lipoprotein Cholesterol (LDL) and Very Low Density Lipoprotein Cholesterol (VLDL) were calculated by Friedewald's equation.[10]Quality control was done by Bio-Rad immunoassay controls. Sensitivity of all the assays was 98% with lowest detection limits.

The results were expressed as mean ± SD and analysed by applying Z test using Microsoft excel 2007.

Results:

Table 1: Comparison of hsCRP and Lipid Profile in different groups:

Parameters	Normotensive Group A (Mean ± SD)	Prehypertensive Group B (Mean ± SD)	Hypertensive Group C (Mean ± SD)
hsCRP (mg/L)	1.31 ± 1.7	1.77 ± 1.3	4.74 ± 3.4**
Cholesterol (mg/dl)	150.7 ± 22.8	171.7 ± 37.2**	165.0 ± 32.5**
Triglycerides (mg/dl)	97.4 ± 43.9	95.2 ± 30.5	122.0 ± 48.5**
HDL-C (mg/dl)	41.56 ± 7.5	44.0 ± 9.4	39.31 ± 9.82**
VLDL (mg/dl)	19.48 ± 8.7	19.0 ± 6.11	24.4 ± 9.7**
LDL (mg/dl)	89.6 ± 16.6	108.6 ± 31.7**	100.9 ± 26.4 **

We found increased levels of hsCRP(4.74±3.4)in hypertensives as compared to normotensives (1.31±1.7). This increase was statistically highly significant (p<0.001).

Table 2 shows correlation of hsCRP with serum lipid profile.

	r value	P value
CHO	0.31	<0.001
TG	0.10	>0.05
HDL	-0.02	>0.05
VLDL	0.10	>0.05
LDL	0.35	<0.001

In our study we didnot find any association of hsCRP levels in prehypertension (1.77±1.3) as compared to normotensives (1.31±1.7) Statistically higher levels of total cholesterol, triglycerides, LDL, VLDL were found in hypertensives than in normotensives. But only total cholesterol and LDL-

C were increased in prehypertensives than normotensives. Serum total cholesterol (r= 0.31, p<0.001) and LDL cholesterol correlates positively with hsCRP (r=0.35, p<0.001).

Discussion: This indicates inflammation is associated with hypertension. Ki Chul Sung and workers found hsCRP to be an independent risk factor for development of hypertension in Korean population.[11]
Sesso and workers found a positive association between increasing levels of CRP and risk of developing hypertension.This association between higher hsCRP and new-onset hypertension led Sesso et al to suggest that hypertension is an inflammatory disease.[12] In a study conducted by Bautista et al in 2003 did not find any association of hsCRP with hypertension. They attributed this to the small sample size of their study.[13] In our study we didnot find any association of hsCRP levels in prehypertension (1.77±1.3) as compared to normotensives (1.31±1.7) which is probably attributable

Though Sesso et al excluded prehypertensives from their study, vast majority of the prehypertensives turned hypertensives during follow-up. They also found that those women who had a higher hsCRP were more likely to develop hypertension.[12]

The ATTICA study found higher levels of hsCRP, TNF-α and other inflammatory markers in prehypertensives. This association was independant of other co-existing risk factors for cardiovascular diseases indicating that prehypertension might be an inflammatory condition.[14]

Similar findings were seen in the POWIRS study by Shutte et al (2006). They found higher levels of hsCRP, fibrinogen and leptin in African women as compared with Caucasians.[15] In another study baseline hsCRP and IL-6 were found to be higher in both cases and control postmenopausal black women as compared to whites.[16]
Lopes et al found similar lipid metabolic alterations in normotensive subjects with positive family history of hypertension.[17]

In the Strong Heart Study (2006), abnormal lipid profile was found to predict development of hypertension in American Indian population. In this longitudinal cohort study, they found that decrease in HDL cholesterol from baseline predicted development of hypertension in 8 year follow up.[18]
In the CARDIA study, development of incident hypertension over 10 years in 5115 black and white young adults was associated with initial systolic BP, levels of triglycerides and HDL-cholesterol.[19]

Rasouli M et al (2006) found higher triglycerides and cholesterol levels in hypertensives.[20] Nah EH and Kim HC (2007) also found higher levels of LDL-cholesterol and lower levels of HDL-cholesterol in prehypertensives than normotensives.[21]

Marco et al in 2009 (the strong heart study data) studied the cardiometabolic predictors of progression of prehypertensives to hypertensives. They found that thoseprehypertensives who developed hypertension had higher levels of inflammatory markers, higher triglycerides and lower HDL cholesterol.[22] CRP increases expression of endothelin-1[23],Plasminogen activator inhibitor-1[24] to promote vasoconstriction, platelet activation and thrombosis. CRP has also shown to upregulate angiotensin receptor-1 thus enhancing angiotensin-II induced rise in blood pressure.[25]Some recent studies underline the possibility that arterial stiffening may precede development of hypertension. Pulse Wave Velocity and augmentation index, a measure of arterial stiffening was associated with many circulating inflammatory markers in recent studies suggesting that inflammation may play a role in arterial stiffness.[26,27,28] All of this data suggest that vascular inflammation plays a role in pathophysiology of hypertension and may potentiate the proatherogenic effects of hypertension.

Conclusion: Atherosclerosis is increasingly being recognised as a chronic inflammatory disease. Hypertension is well-established risk factor for atherosclerosis. Increased levels of hsCRP in hypertension implies a role of inflammation in hypertension. But whether inflammation is a cause or effect of hypertension is not clear from this study. Inflammation maybe the bridge that

connects proatherosclerotic effects of hypertension to future CVD complications in hypertension. Elevated CRP levels in addition to lipid profile screening may be a valuable tool to predict future CVD risk.

Limitation of the study: Due to the cross-sectional nature of our study and a small sample size, findings of our study need to be confirmed in larger prospective study. We didnot follow-up the prehypertensive group for development of hypertension. Therefore, whether inflammation is a cause or effect of hypertension cannot be concluded from this study.

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