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Original Research Article

A Study of Conventional Risk Factors of Metabolic Syndrome in Hypertensive Subjects and their Probable Correlation with Blood C-Reactive Protein and Fibrinogen Level

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Abstract

Background: Hypertension is one of the most important risk factors for cardiovascular disease and has become an increasingly important contributor to the global health burden. Mostly hypertension is idiopathic. Recently, chronic low-grade inflammation has been identified as an integral part in the pathogenesis of vascular disease. Present study was planned to investigate the level of acute phase reactants in hypertension & their correlation with conventional risk factors of metabolic syndrome.

Materials & Methods: It was a case-control observational study. All subjects were divided in two groups 100 hypertensive and 100 healthy controls, between 30-60 years of age, of either gender. Standard protocol had been followed to analyze biochemical parameters on Biochemistry Fully auto-analyzer EM-360 by TRANSASIA. Data were collected and subjected to statistical analysis using Statistical Package for the Social Sciences (SPSS trial version 16.0).

Results: Statistical analysis showed that the hypertension significantly affects blood sugar and lipid levels. Hypertensive subjects had significantly elevated level of blood sugar, triglycerides, total cholesterol and LDL cholesterol and significantly lower HDL cholesterol level as compare with Non-hypertensive subjects. The mean serum CRP levels were significantly higher in subjects with hypertension compared with control group of healthy subjects (17.27±12.24mg/l versus 8.28±5.78mg/l, $p<0.05$). Similarly mean plasma fibrinogen levels were also significantly higher in hypertensive compared with control group (470.6±150.9mg/dl versus298.54±113.6mg/dl, $p<0.05$).

Conclusion: The elevated concentration of inflammatory markers observed in present study indicates major role of inflammation in development of hypertension.

Keywords: Hypertension, C - Reactive Protein, Fibrinogen, Auto-analyzer

Introduction

Metabolic syndrome (MetS) is a sum of metabolic abnormalities that give rise increased risk of cardiovascular disease (CVD) and diabetes mellitus (DM). The major features of the metabolic syndrome include central obesity, hypertriglyceridemia, low HDL cholesterol, hyperglycaemia, and hypertension. Chronic pro-inflammatory and prothrombotic states have also been considered to this syndrome. National Cholesterol Education Program Adult Treatment Panel III recommended the use of five variables including waist circumference, serum triglycerides level, serum HDL cholesterol level, blood pressure and fasting glucose level. Subject meeting three of these five criteria were classified as having MetS. Insulin resistance has been considered a key feature of the metabolic syndrome by W.H.O.[1,2].

Hypertension is an important risk factors for heart ailments and has become a major culprit to the global health burden[3,4]. By 2025, the number of people with hypertension will increase by about 60% to a total of 1.56 billion as the proportion of elderly people will increase significantly[5]. The prevalence of hypertension in India 59.9 and 69.9 per 1000 in males and females respectively in urban population[6] and 35.5 and 35.9 per 1000 in males and females respectively in the rural population[7].

Mostly hypertension is idiopathic but pathogenesis of vascular disease is influenced by chronic low-grade inflammation[8,9]. Many clinical studies on hypertensive subjects have demonstrated elevated concentration of well documented pro-inflammatory markers (like high sensitive C-reactive protein [hsCRP], Interleukin (IL)-6, IL-1β, Tumour Necrosis Factor Alpha (TNF-α) and Angiotensin II (Ang II) [10].

High hs-CRP level is a future risk factor of the development of hypertension in pre-hypertensive and normotensive subjects[11,12]. Experimental and clinical observations indicate inflammation and rise of inflammatory markers like C-reactive protein, fibrinogen as an important pathogenic mechanism in obesity-associated MetS[13,14].

Our work was related to two important inflammatory markers CRP and fibrinogen. C-reactive protein and Fibrinogen found in the blood, the levels of which rise in response to inflammation. CRP has strong affinity towards phosphocholine present on the surface of dead or dying cells. This action activates the complement system via C1Q complex[15].

In the view of the probable involvement of the acute phase reactants (APR), present study was planned to investigate the level of APR in hypertension & their correlation with conventional risk factors of metabolic syndrome.

Material and Methods

This was a case-control observational study conducted between July to Dec 2019 in the Biochemistry Laboratory of a tertiary care hospital. For this study subjects between 30-60 years of age, of either gender, were selected and screened for hypertension according to new guidelines and divided according to blood pressure in 2 groups of hypertensive and non-hypertensive. Each group comprised of 100 subjects.

Ethical statement: Approval of the study has been taken from the Institutional ethics

committee. Informed consents were obtained in written form from patients and all clinical investigation was conducted according to the principles expressed in the Declaration of Helsinki. The patients gave consent for the publication of the clinical details.

Inclusion criteria:

- Clinically diagnosed hypertensive subjects
- Age group- 30- 60 years.
- Either gender male and female

Exclusion criteria:

- Patients with cardiac, respiratory, renal, hepatic or neurologic disease, rheumatoid arthritis, Gastrointestinal or Renal disorder, pregnancy, acute or chronic inflammatory conditions
- Patients below 30yrs or above 60yrs
- Local or systemic sepsis.

Physical Examination

All the subjects had undergone through a complete physical examination. The family history regarding obesity, diabetes, hypertension, coronary artery disease was carefully recorded by a questionnaire.

Collection and analysis of sample

After overnight fasting, 5ml of venous blood in BD plain vacutainer (Becton Dickinson and company, Franklin Lakes, USA) of the subjects was drawn from anticubital vein using aseptic techniques for the estimation of blood sugar, lipid profile and C-reactive protein and for measurement of Fibrinogen, samples were collected in 2.7 ml blue-top BD vacutainer containing 3.2% sodium citrate. After 30-60 minutes of collection samples were centrifuged and serum and platelets poor plasma was obtained. Analysis was done on fully auto Biochemistry Analyzer-Transasia-EM-360 using internal quality control of RANDOX.

LDL cholesterol is calculated from Friedewald's equation if triglycerides is up to 400mg/dl, if triglycerides is more than 400mg/dl, LDL is measured by Direct LDL method.

Participants were subjected to updated NCEP ATP III criteria for assessment of metabolic syndrome.

Updated NCEP ATP III Criteria:

1. Elevated waist circumference: Men — equal to or greater than 90 cms., Women — equal to or greater than 80 cms (According to New guidelines created by the Indian Ministry of Health).
2. Elevated triglycerides: Equal to or greater than 150 mg/dl
3. Reduced HDL ("good") cholesterol: Men — Lower than 40 mg/dl, Women — Lower than 50 mg/dl.
4. Elevated blood pressure: Equal to or greater than 130/85 mm Hg or use of medication for hypertension.
5. Elevated fasting glucose: Equal to or greater than 100 mg/dl or use of medication for hyperglycemia.

Subjects having three of these five criteria's were designated as metabolic syndrome's subjects

Data entry and Statistical analysis

Results were expressed as Mean ± SD. Collected data were coded and analyzed with the help of using Statistical Package for the Social Sciences (SPSS trial version 16.0). Student's t-test, and strength of association between two variables were measured by Pearson's correlation coefficient (r). P values < 0.05 was considered as statistically significant.

Results

Table 1: Comparison of Blood Sugar and Lipid Parameters of between Groups

Parameters	Non-hypertensive (Group-1)	Hypertensive (Group2)	Unpaired t-test	
			t-score	P-value
Fasting Blood Sugar (mg/dl)	83.6±14.6	96.7±12.5	4.8	P<0.0001 Significant
Triglycerides (mg/dl)	124.46±23.5	140.58±32.1	2.86	P =0.005 Significant
Total Cholesterol (mg/dl)	183.62±50.78	227±47.7	4.4	P<0.0001 Significant
LDL-Cholesterol (mg/dl)	114.62±51.82	156.45±49.86	4.1	P<0.0001 Significant
HDL-Cholesterol (mg/dl)	47.1±9.0	41.36±7.47	3.4	P=0.0008 Significant
Total Cholesterol /HDL Ratio	4±1.47	5.34±1.91	3.93	P=0.0002 Significant
LDL/HDL Ratio	2.48±1.4	3.72±1.78	3.8	P=0.0002 Significant
TG/HDL Ratio	2.74±.89	3.0±1.0	1.37	P=0.17Not Significant

Values are Mean ± SD

Table 1 shows blood sugar and lipid parameters of Non-hypertensive and hypertensive subjects. Statistical analysis shows that the hypertension significantly affects blood sugar and lipid levels. Hypertensive subjects had significantly elevated level of blood sugar, triglycerides, total cholesterol and LDL cholesterol and significantly lower HDL cholesterol level as compare with Non-hypertensive subjects. Further CAD risk prediction ratio - Total Cholesterol/HDL, LDL/HDL and TG/HDL ratio has progressively increased from Non-hypertensive to Hypertensive group indicate that Hypertensive subjects are at relatively greater risk for developing cardiovascular diseases as compared to subjects in Non-hypertensive group.

Table 2: Comparison of C-reactive protein and Fibrinogen Levels of both Groups

Parameters	Non-hypertensive subjects (Group-1)	Hypertensive Subjects (Group2)	Unpaired t test	
			t-score	P-value
C-reactive protein (mg/l)	8.28±5.78	17.27±12.24	4.7	P<0.0001 Significant
Fibrinogen (mg/dl)	298.54±113.64	470.6±150.9	6.4	P<0.0001 Significant

Values are Mean ± SD

Table 2 shows that C-reactive protein and fibrinogen level are significantly elevated in hypertensive subjects as compared to Non-hypertensive subjects. C-reactive protein and fibrinogen are positive acute phase reactants and their levels increased during inflammation.

Correlation Analysis of study Parameters:

Table 3: Correlation of Systolic Blood Pressure with C-reactive protein, Fibrinogen, HDL, LDL, and Triglycerides in Hypertensive subjects

Parameters	Systolic Blood Pressure (Hypertensive subjects)	
	r-score	p-value
C-reactive protein	0.43	0.001 Significant
Fibrinogen	0.22	0.12 Not Significant
HDL	-0.30	0.03 Significant
LDL	0.61	<0.0001 Significant
Triglycerides	0.40	0.003 Significant

It has been concluded from table 3 that both acute phase reactants have positive correlation with Systolic blood pressure but only C - reactive protein has significant correlation.

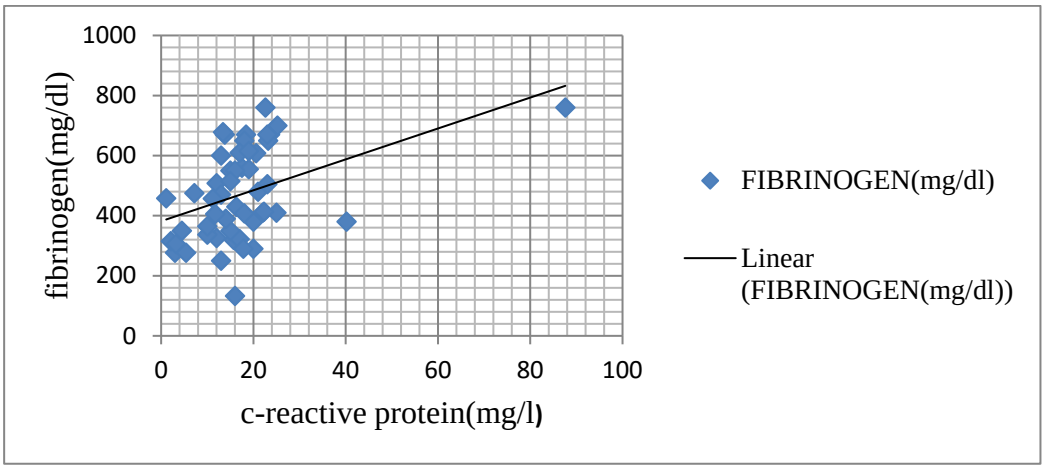

Figure 1: Correlation of C-reactive protein and Fibrinogen in hypertensive subjects

Figure 1 showing both acute phase reactants are elevated in cases (hypertensive), supporting inflammatory pathology of hypertension.

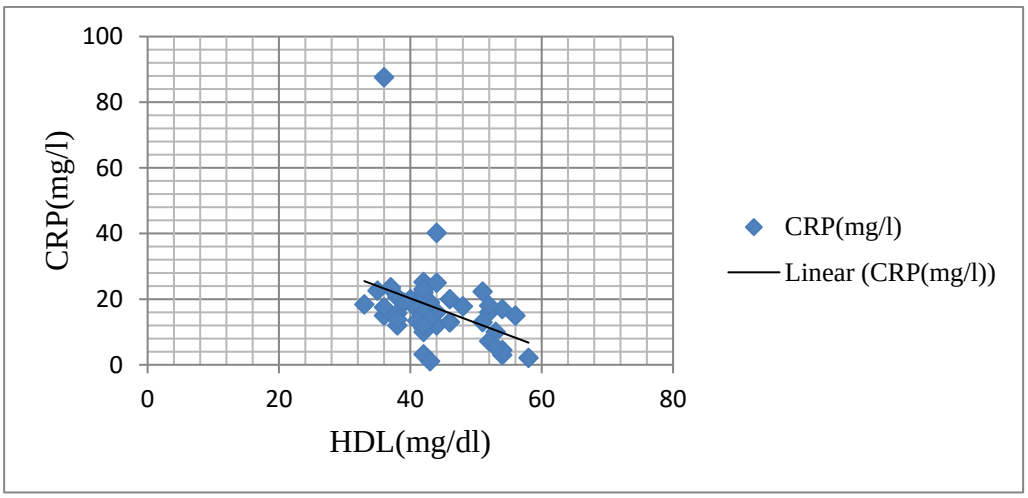

Figure 2: Correlation of C-reactive protein and HDL in hypertensive subjects

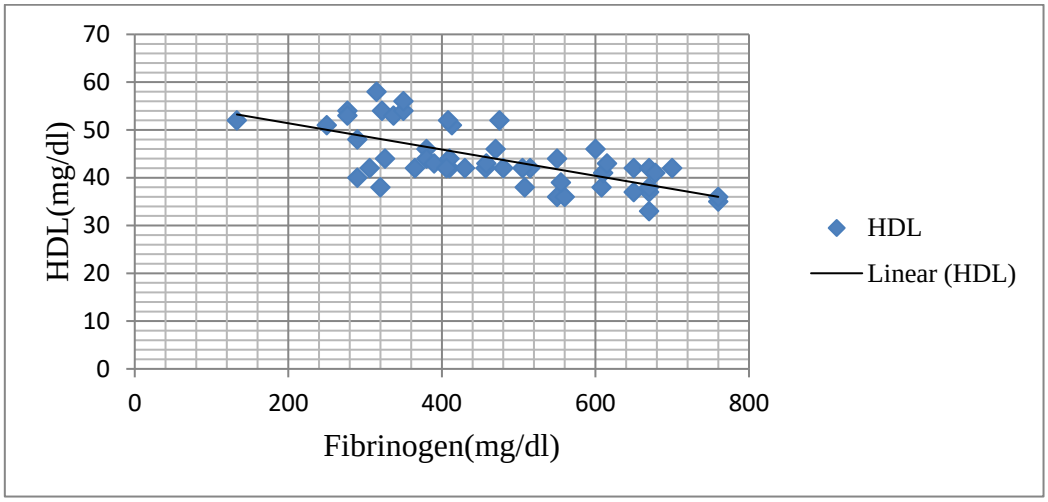

Figure 3: Correlation of Fibrinogen with HDL in hypertensive subjects

Figure 2 and 3 showing that c- reactive and fibrinogen has significant negative correlation with high density lipoprotein. Therefore increment in the level of these acute phase reactants is a risk factor for cardiovascular disease.

Discussion

Hypertension is one of the most common public health problems of the 21st century which increases morbidity and mortality in both developing and developed worlds. Hypertension is a positive risk factor in the development of dyslipidaemia, DM, CVD etc. Hypertension is one of the important components of metabolic syndrome, which is a cluster of clinical and metabolic abnormalities including abdominal obesity, insulin resistance, hypertension, dyslipidaemia and all these factors directly increases the risk of CVD.

American Association of Endocrinology does not consider obesity as a component and highlights the importance of insulin resistance to the syndrome[16] whereas National Cholesterol Education Program (NECP): Adult Treatment Panel III (ATP III) gives equal weightage to any of the components of the syndrome: glucose intolerance, obesity, hypertension and dyslipidaemia[17]. It is now very clear that insulin resistance and obesity are two important component of metabolic syndrome.

The present study was conducted to study evaluate the conventional risk factors of

metabolic syndrome in hypertensive subjects. Hypertension was defined as a reading of ≥140/90 mmHg on three consecutive measurements at least six hours apart. Subjects were distributed on the basis of increasing blood pressure in 2 groups (each has 100 subjects) of nonhypertensive and hypertensive.

The observations of present study also revealed that the hypertension significantly affects blood sugar and lipid levels. Hypertensive subjects had significantly elevated levels of blood sugar and deranged lipid profile (high triglycerides, total cholesterol and LDL cholesterol and low HDL cholesterol level) as compare to nonhypertensive subjects. (**Table-3 & Figure 2, 3**) Further CAD risk prediction ratio - Total Cholesterol/HDL, LDL/HDL Ratio has significantly elevated in hypertensive group indicate that hypertensive subjects are at relatively greater risk for developing cardiovascular diseases as compared to subjects in nonhypertensive group (**Table 1**).

Essential hypertesion is regarded as a multi-factorial condition. This fact is supported by many cross-sectional studies that demonstrate familial aggregation of the disorder despite different environmental factors. This information gives us genetic basis of the disease and new approaches to its treatment and prevention[18,19].

It is thoroughly studied that various clinical signs and symptoms of the metabolic syndrome are associated with systemic inflammatory response[13,14], and a link between hypertension and inflammation has been established in many research works[10,11]. C-reactive protein & Fibrinogen are important positive acute phase proteins & mounting of which may contribute to metabolic abnormalities & insulin resistance[20].

In present study it has also been observed that there is significant elevation of inflammatory markers (acute phase reactants) C-reactive protein and Fibrinogen in hypertensive subjects as compare to nonhypertensive subjects (**Table 2 & Figure 1**). There was almost 2 times elevation in C-reactive protein level in hypertensive subjects (**Table 2**). Blood concentration of this acute phase reactant was found to have significant positive correlation with systolic blood pressure. (**Table 3**)

Limitation: As prevalence of hypertension is very high. Therefore this study needs larger sample size and funding resources to get generalizable results.

Conclusion

All of the components of the dyslipidaemia, including higher triglycerides and decreased HDL levels, as observed in present study, have been shown to be atherogenic. Chronic low-grade inflammation has been associated with the pathogenesis of vascular disease. The presence of inflammatory markers like C-reactive protein, fibrinogen, TNF-α, IL-6 within the body can have a significant role in the development and progression of many disease processes like CVD, cerebrovascular accident, and diabetic complications. The elevated concentration of inflammatory markers observed in present study indicates major role of inflammation in development of hypertension. It can also be considered that hypertension is an inflammatory process.

Abbreviation

MetS	Metabolic Syndrome
CRP	C-Reactive Protein
IL-6	Interleukin-6
IL- 1β	Interleukin-1β
TNF-α	Tumour Necrosis Factor-α
APR	Acute Phase Reactants

Conflict of interest: there is no conflict of interest between authors.

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Recommendation: we recommends further study on etiological role of other inflammatory markers like TNF-α, IL-6, IL- 1β, ferritin in hypertentive patients.

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