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Evaluation of a Fibrinogen, Total Antioxidant Capacity and Body Mass Index in Essential Hypertensive Men.

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ABSTRACT

Recent studies indicate that the pro-inflammatory action of Fibrinogen or the activation of inflammatory sensitive proteins contribute to the increased risk of Essential hypertension (HTN). Hence the objective of the study was to evaluate serum levels of Fibrinogen, Total Antioxidant Capacity (TAC) and body mass index (BMI) in essential hypertensive men and to compare these with the normotensive men. A prospective case control study was conducted, the subjects were divided into the following two groups. Group A: 30 male patients with essential hypertension, Group B: 30 male, healthy individuals. Serum TAC and BMI were estimated and BMI was calculated in both cases and controls. The values obtained were expressed as Mean ± SD and was compared by using student 't' test. Correlation was found between BMI, TAC and Fibrinogen. The mean age and SD of controls and cases were 43.67±11.74 and 50.12±11.47 years respectively. Mean and SD of serum Total anti-oxidant capacity and Fibrinogen levels for controls and cases as 167.76 ± 40.40 and 99.97 ± 38.11; 234.313 ± 51.35 and 347.27 ± 79.79 respectively mg/dl and respectively in controls & cases. BMI was calculated and found to be 21.07 ± 2.25 in controls and 28.20 ± 3.55 in cases and were statistically significantly ($p<0.001$) altered in determining severity of essential hypertension. These data indicate that Evaluation of Serum Fibrinogen, BMI and TAC levels shall influence the process of subclinical inflammation involved in the increased risk of Essential hypertension.

Keywords: Essential hypertension, Fibrinogen, Total antioxidant capacity, Body mass index.

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INTRODUCTION

Vascular dysfunction is a highly complex biological process, and cardiovascular diseases are a leading cause of morbidity and mortality in the India [1]. In India the prevalence of hypertension as per World Health Organisation's global health statistics 2012, 23.10 per cent men over 25 years old and globally, the overall prevalence of raised blood pressure in adults aged 25 and over, rose from 600 million in 1980 to nearly 1 billion in 2008 [2]. It has a large impact on disease incidence, and can be controlled by early measurement of blood pressure by using Sphygmomanometer. This is the only method available for diagnosis of hypertension. Recent studies have showed that inflammatory sensitive proteins levels are associated with future increase in systolic blood pressure and pulse pressure [3].

In recent years a series of epidemiological studies has show fibrinogen values are reported to be shown that high fibrinogen levels represent a risk elevated in arterial hypertension, where they are often factor for cardiovascular morbidity and mortality [3]. Additionally, fibrinogen and its derivatives seem to be-involved in both the initiation and sustained growth of atherosclerotic lesions

The oxidative stress prevalent in essential hypertension is augmented by obesity. Excessive formation of reactive oxygen species (ROS) in essential hypertension, leads to endothelial dysfunction, an early event of atherogenesis. The increase in oxidative stress in obesity probably leads to hypertension through increased vascular tone [8]. Oxidative stress is defined as a disturbance in the balance between the antioxidants and prooxidants with increased levels of prooxidants leading to potential damage. To circumvent the damage caused by oxygen free radicals, a team of endogenous and exogenous antioxidant constituting total antioxidant capacity (TAC) is present in human serum. Hence, the aim of the study was to evaluate the role of Fibrinogen , Total antioxidant capacity and BMI in essential hypertensive men.

MATERIALS AND METHODS

A case control study was conducted on patients attending outpatient department of Medicine M.S. Ramaiah Teaching Hospital, Bangalore. Total of sixty subjects were included in the study. The subjects were divided into two groups, each group consisting of 30 subjects. 30 cases included in this study were clinically diagnosed essential hypertensive male patients between the age of 30 – 70 years with the duration of essential hypertension upto 10 years with or without treatment. Systolic pressure ≥ 140 mmHg and a diastolic pressure ≥ 90mmHg on an average of 2 readings on 2 different occasions [7]. Thiry healthy male individuals with systolic pressure < 130mmHg and diastolic pressure <85 mmHg, between the age group of 30-70 years were included as controls.

Essential hypertensive patients on medications like steroids, antioxidants, vitamins, which will affect the oxidative stress. Patients who were tobacco users and alcoholics and subjects with renal disorders / hepatic disorders/ secondary hypertensive patients were excluded from this study. Complications due to hypertension like cardiovascular disease, retinopathy, nephropathy, stroke and diabetes mellitus. Institutional ethics committee clearance was obtained prior to the study and informed consent was obtained from the subjects participating in this study.

METHODOLOGY

Blood pressure was recorded using sphygmomanometer as a measure of hypertension. Systolic pressure of <130 mmHg and diastolic pressure of <85 mmHg was considered normal. BMI of <25 kg/m^2 was considered normal. Height was measured on a clinic stadiometer. The body weight was assessed using a calibrated weighing scale, with subjects using light clothes and no shoes. The body mass index (BMI) was calculated as body weight (kg) divided by square height (m2) and BMI of <25kg/m2 was considered normal. Blood pressure was measured using sphygmomanometer three times after the subject had been seated for 5 minutes, and the mean of the last two readings was used for analysis. Systolic pressure of <130 mmHg and diastolic pressure of <85 mmHg was considered normal. All subjects were asked to fast overnight for 10 hours before blood specimen collection. Aseptic precautions were taken while collecting venous blood samples from all the subjects for the estimation of Serum Fibrinogen and total antioxidant capacity. The sample was collected in plain vacutainer, allowed to clot for 10 minutes and centrifuged. The serum was separated and immediately stored at -20°C, till the analysis. Serum samples were thawed to room temperature before the analysis. Calibration and the controls were run prior to estimation of serum Fibrinogen Plasma fibrinogen was

estimated using classical Clauss method by semi autoanalyzer using Transasia instrument in metropolis laboratory, M.S.Ramaiah memorial hospital, Bangalore. Estimation of serum total antioxidant capacity was carried out by FRAP- ferric reducing ability of plasma assay by using spectrophotometer (ELICO) [9]

STATISTICAL ANALYSIS

Data was analyzed using SPSS software version 17.0. It was considered $p<0.05$ as statistically significant value. Descriptive statistics of Fibrinogen, TAC and BMI was analyzed and expressed in Mean and SD. Independent t test was used to compare the mean Fibrinogen, TAC and BMI between cases and controls after making the log transformation, since the data distribution was not normally distributed (skewed). Pearson's correlation coefficient was used to find the strength of relationship between the BMI and Fibrinogen, TAC and its significance was estimated using independent t –test

RESULTS

Thirty essential hypertensive men, within the age group of 30 to 70 years considered as cases and women were not included in this study because of hormonal changes and their potential effects on inflammatory markers after menopause. Thirty age matched healthy males were considered as controls. The mean age and SD of controls and cases were 43.67 ± 11.74 and 50.12 ± 11.47 years respectively. Mean and SD of serum TAC was 167.76 ± 40.40 in controls and 99.97 ± 38.11 in cases, statistically significant lowered levels ($P<0.001$) in cases compare to controls. CRP was 0.62 ± 0.83 and 2.77 ± 3.58 respectively in controls & cases, statistically significant raise in cases compare to controls ($P<0.001$). BMI was calculated and found to be 21.07 ± 2.25 in controls and 28.20 ± 3.55 in cases and were statistically significantly($P<0.001$). (Table 1). The Pearson's correlation was studied for each parameter in cases and it was observed that, there was a statistically significant positive correlation between BMI and CRP ($r=0.53$, $P <0.001$). It was also found that the there was a statistically significant negative correlation between BMI and TAC ($r= -0.45$, $P<0.001$). However the strength of the relationship was not good. There was negative correlation found between CRP and TAC but it was statistically not significant ($r= -0.22$,$P>0.05$)

Table 1: Serum Total antioxidant Capacity,Plasma Fibirnogenlevels and BMI in hepertensive men and healthy controls.

Parameter	Control	Cases	P value
TAC	167.76 ± 40.40	99.97 ± 38.11	<0.001*
Plasma Fibrinogen	0.62 ± 0.83	2.77 ± 3.58	<0.001*
BMI	21.07 ± 2.25	28.20 ± 3.55	<0.001*

*Statistically significant (P value < 0.001)

DISCUSSION

Recent advances have established a fundamental role for inflammation in mediating all stages of essential hypertension from initiation through progression and, ultimately, the thrombotic complications of atherosclerosis [9]. These new findings provide important links between risk factors and the mechanisms of atherogenesis. Elevations in markers of inflammation are known to predict outcomes of patients with acute coronary syndromes, independently of myocardial damage.

Hypertension is one of the classical risk factors for atherosclerosis. Increasing evidence supports the view that inflammation may participate in atherosclerosis in hypertension providing a pathophysiological basis. Hypertension is a leading risk factor that predisposes to increased cardiovascular morbidity and mortality, and is additionally an important risk factor for development of chronic kidney disease in the presence of obesity. Any reduction in blood pressure is likely to reduce the risk of complications. The incidence of clinical complications were significantly associated with raised systolic blood pressure [11].

BMI of >23 was considered in the overweight and obese category according to standard for Asians. BMI is a measure of relative weight, which correlates highly with percentage of body fat and is largely independent of height. BMI is dependent on environmental factors such as physical activity and culture. BMI cut off points are used clinically to identify individuals for absolute risk assessment of various disorders like CVD and type-2-DM. The proportion of Asians with a high risk of type-2-DM and CVD is substantial at BMI

lower than existing WHO cut off points for overweight (≥ 25kg/m^2) [12]. It has been observed in this study the comparison of mean BMI in cases and controls were 234.313 ± 51.35 and 347.27 ± 79.79 respectively and statistically significant increase in cases compare to controls (P< 0.001).

Plasma Fibrinogen levels in the top third exhibited 2-fold increase in future vascular events even after adjustment for all other available vascular risk factors [15]. Perhaps of equal clinical impact, both men and women with elevated levels of Plasma Fibrinogen consistently show high vascular risk, even in the absence of hyperlidipidemia. Algorithms that combine Plasma Fibrinogen and lipid screening to improve risk assessment may have clinical utility for outpatient use.

Total antioxidant capacity was reduced in essential hypertension patients as compared to controls indicating the existence of high levels of oxidative stress and the requirement of more antioxidants to combat the stress. In a study conducted by Jaun J et al. it was seen that vitamin C concentration was low in essential hypertension and are associated with inflammation and the patient's functional state [16]. Low grade inflammation in atherosclerosis may be associated with oxidative stress and resultant decrease in vit C concentration [17]. In a study conducted by Shimoni et al. it was seen that increased stress could be one of the factors leading to cardiovascular disease in Essential hypertension patients [18]. Free radical activity and oxidative damage have been implicated in the initiation of vascular disease, and antioxidants provide the first line of defense against free radicals. Several studies have shown that episodes of ischemia –reperfusion can reduce the total antioxidant capacity [19]. Study by Margarita L et al, Serum levels of TAC had a negative significant correlation with hypertensive pts with stroke with r = 0.348, P = 0.051 [20]. It is possible, therefore, that the longer or more severe the bouts of ischemia, greater the reduction in the total antioxidant capacity and subsequent increase in the risk of developing infective complications. In fact it has been shown that antioxidant defenses in Essential hypertension patients are lower than age matched controls. If these patients have an unimpaired nutritional status with low total antioxidant capacity, they may benefit from antioxidant supplementation.

Chrysohoou et al, reported that obese or overweight participants had lower TAC concentrations compared to normal individuals [21]. Lower TAC may partially explain their increased risk for diabetes and chronic hypertension. Uric acid was found to be elevated in both obese and metabolic syndrome patients, but significantly higher in patients with metabolic syndrome [22]. Uric acid contributes to 60% of the total antioxidants estimated by FRAP assay, while ascorbic acid contributes 15% , protein 10%, others by 5%. The present study shows that obesity with hypertension in cases has elevated levels of oxidative stress reflected as decreased levels of TAC. In obesity, the adipocyte plays a central role in the balance or imbalance of metabolic homeostasis. In obesity, hypertrophic adipocyte is challenged by many insults, including surplus energy, inflammation, and elevated oxidative stress.

The proinflammatory state of obesity and chronic hypertension may also originate due to excessive caloric intake [23] .Oxidative stress is caused by the presence of free radicals or radical generating agents in concentrations that overwhelm natural radical blocking or scavenging mechanisms. These free radicals react with cellular constituents forming products like hydroperoxides, MDA, protein carbonyl etc [24]. Inflammatory cytokines released by adipocytes can also induce and worsen oxidative stress. The increased levels of oxidative stress and chronic sub clinical inflammatory state seen in chronic hypertensive patients leads to higher risk of atherosclerotic and other cardiovascular complications. Thus, the estimation of TAC can be used as a valuable tool to evaluate the level of oxidative stress in obesity and chronic hypertension. The state of elevated oxidative stress can be a potential target for preventive and therapeutic interventions prior to development of complications.

CONCLUSION

In the present study, it has been found that serum Plasma Fibrinogen levels are raised in essential hypertension while the TAC has decreased. The role of plasma Fibrinogen as pro atherogenic factors has already been described. Further studies on a larger sample sizes with similar findings may establish serum Plasma Fibrinogen as biomarkers to predict future coronary events.

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