COMPARE AND CORRELATE PLASMA FIBRINOGEN, TOTAL ANTIOXIDANT CAPACITY AND BODY MASS INDEX IN PREDIABETES AND NORMAL INDIVIDUALS

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ABSTRACT

Current studies indicate that the pro-inflammatory action of Fibrinogen or the activation of inflammatory sensitive proteins predicts to the increased risk of pre-diabetes. Thus objective of the project was to be evaluate plasma levels of Fibrinogen, Total Antioxidant Capacity (TAC) and Body Mass Index (BMI) in pre-diabetes and to compare these with the normal men.

A prospective case control project was conducted, the subjects were divided into the following two groups. Group A: 34 male patients with pre-diabetes, Group B: 34 male, healthy individuals. Serum TAC and BMI were evaluated and BMI was calculated in both cases and controls. The results 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 54.67±11.74 and 51.12± 11.47 years respectively. Mean and SD of serum Total antioxidant capacity and Fibrinogen levels for controls and cases as 263.313±51.35 and 377.27±79.79 respectively mg/dl and respectively in controls and cases. TAC levels for controls and cases as 187.76±40.40 and 89.97±38.11 respectively mg/dl and respectively in controls and cases.

BMI was calculated and found to be 22.07±2.25 in controls and 29.20±3.55 in cases and were statistically significantly ($p<0.001$) altered in predicting severity of pre-diabetes. These data indicate that evaluation of Plasma Fibrinogen, BMI and TAC levels might predisposing the process of subclinical inflammation predisposing in the increased risk insulin resistance and thereby of pre-diabetes.

KEYWORDS

Pre-diabetes, Fibrinogen, Total antioxidant capacity, Body mass index.

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INTRODUCTION: Metabolic syndrome is a highly complex biological process and metabolic syndrome diseases are a leading cause of morbidity and mortality in the India.[1] In India the prevalence of pre-diabetes as per World Health Organisation's global health statistics 2012, 23.10 percent men over 25 years old and globally the overall prevalence of metabolic syndrome in adults aged 25 and over rose from 600 million in 1980 to nearly 1 billion in 2008.[2] Present studies have showed that inflammatory sensitive proteins levels are linked with future predicting increase in diabetes.[3] In current years a series of epidemiological studies have shown fibrinogen values are reported to be shown that high fibrinogen levels represent a of risk metabolic syndrome, where they are often factor for metabolic syndrome morbidity and mortality.[4] Many mechanisms might contribute to the metabolic syndrome risk factors. These include increased blood viscosity, obesity, dyslipidaemia etc., enhanced platelet adhesiveness and aggregation favoring the deposition of thrombus decreased perfusion and tissue oxygenation in addition fibrinogen and its derivatives seem to be involved in both the initiation and continued growth of atherosclerotic lesions.

Oxidative stress in pre-diabetes is augmented by obesity.[5] Disproportionate formation of Reactive Oxygen Species (ROS) in pre-diabetes leads to endothelial dysfunction and premature event of atherogenesis. Oxidative stress is defined as a disorder in the balance between the antioxidants and pro-oxidants with amplified levels of pro-oxidants leading to potential damage. To avoid the damage caused by oxygen free radicals, a band of endogenous and exogenous antioxidant makes the Total Antioxidant Capacity (TAC), which is present in human serum.[6] Thus, the aim of the present project was to evaluate the role of fibrinogen, total antioxidant capacity and BMI in pre-diabetes.

MATERIALS AND METHODS: A case control project was conducted on patients attending out-patient department of Medicine Sapthagiri Institute of Medical Sciences and Research Centre, Bangalore. Total of sixty eight subjects were included in the study. The subjects were divided into two groups, each group consisting of 34 subjects; 34 cases included in this project were clinically diagnosed pre-diabetes male patients between the age of 30–70 years with the extent of pre-diabetes up to 10 years with or without treatment. Thirty four healthy male persons between the age group of 30-70 years were included as controls.

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Pre-diabetes patients on medications like steroids, antioxidants, vitamins, which will involve the oxidative stress. Patients who were tobacco users and alcoholics and subjects with renal disorders/ hepatic disorders/ secondary hypertensive patients were disqualified from this study. Impediments due to pre-diabetes like metabolic syndrome disease, retinopathy, nephropathy, stroke and diabetes mellitus. Institutional ethics committee clearance was obtained prior to the project and informed consent was obtained from the subjects participating in this study.

METHODOLOGY: Height was calculated on a clinic stadiometer. The body weight was evaluated using a calibrated weighing scale, with subjects using light clothes and no shoes. The Body Mass Index (BMI) was considered as body weight (kg) divided by square height (m2) and BMI of <25kg/m2 was considered normal. The entire subjects were requested to fast overnight for 10 hours before blood specimen collection. Aseptic safety measures were taken while collecting venous blood samples from all the subjects for the evaluation of Plasma Fibrinogen, FBS, PPBS and total antioxidant capacity. The sample was draw t in plain vacutainer, let to clot for 10 minutes and centrifuged. The serum was separated and instantly stored at -20°C, till the analysis. Serum samples were thawed to room temperature prior to the examination. Calibration and the controls were processed prior to estimation of Plasma fibrinogen was calculated using classical Clauss technique by semi-autoanalyzer.[7]

Sapthagiri Institute of Medical Sciences and Research Centre, Bangalore. Assessment of serum total antioxidant capacity to be carried out by FRAP- ferric reducing ability of plasma assay by using spectrophotometer.[8]

STATISTICAL ANALYSIS: Records were evaluated using SPSS software version 17.0. It was considered $p<0.05$ as statistically significant value. Descriptive statistics of fibrinogen, TAC and BMI was evaluated and stated in mean and SD. Independent t test was employed to compare the mean fibrinogen, FBS, PPBS, TAC and BMI between cases and controls after creating the log transformation, because the data distribution was not normally dispersed (skewed). Pearson's correlation coefficient was used to discover the strength of relationship between the BMI and fibrinogen, TAC and its significance was evaluated using independent t –test.

RESULTS: Thirty four pre-diabetes within the age group of 30 to 70 years evaluated as cases and women were not considered in this project due of hormonal changes and their latent effects on inflammatory markers after menopause. Thirty Four age matched healthy males were evaluated as controls. The mean age and SD of controls and cases were 53.67±11.74 and 51.12±11.47 years respectively. Mean and SD of serum TAC was 263.313±51.35 and 377.27±79.79 cases and control statistically significant lowered levels ($P<0.001$) in cases compared to controls. BMI was measured and found to be 22.07±2.25 in controls and 29.20±3.55 in cases and were statistically significantly ($p<0.001$). (Table 1). The Pearson's correlation was evaluated for each parameter in cases and it was evaluated that there was a statistically significant positive correlation between BMI and fibrinogen ($r=0.53$, $P <0.001$). It was also evaluated that 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 excellent. There was negative correlation between CRP and TAC, except it was statistically not significant ($r=-0.22$, $P>0.05$).

DISCUSSION: Current advances have evaluated an important role for inflammation in the mediation of all phases of pre-onset diabetes all the way through progression and in the end diabetes complications.[9] These fresh findings provide significant links between risk factors and the mechanisms of atherogenesis. Increased in markers of inflammation are recognized to forecast outcomes of patients with acute coronary syndromes, independently of myocardial damage.

Pre-diabetes is one of the standard risk factors for atherosclerosis. Increasing confirmation supports the view that inflammation might participate in atherosclerosis in pre-diabetes establishing a pathophysiological basis.[10] Diabetes is a most important risk factor that predisposes to increased metabolic syndrome morbidity and mortality and is also a major risk factor for the growth of chronic kidney disease in the incidence of obesity.[11]

BMI of >23 was evaluated in the overweight and obese category according to standard for Asians. BMI is a measure of relative weight, which associates highly with percentage of body fat and is largely independent of height. BMI is dependent on ecological factors such as physical activity and culture. BMI cut off points are used clinically to recognize individuals for absolute risk assessment of a range of disorders like CVD and type-2-DM. The section of Asians with a high risk of type-2-DM and CVD is substantial at BMI lower than available WHO cut off points for overweight ($\geq 25 kg/m^2$).[12] It has been seen in this project the comparison of mean BMI in cases and controls were 263.313±51.35 and 377.27±79.79 respectively and statistically significant increase in cases compared to controls ($P<0.001$). TAC levels for controls and cases as 187.76±40.40 and 89.97±38.11 respectively mg/dl and respectively in controls and cases.

Plasma fibrinogen levels in the top third exhibited 2-fold augment in future vascular events even after change for all other available vascular risk factors.[13]

Total antioxidant capacity was reduced in pre-diabetes patients as compared to controls representing the continuation of high levels of oxidative stress and the obligation of more antioxidants to combat the stress. In a project performed by Jaun J, et al. it was seen that vitamin C concentration was low in pre-diabetes and are connected with inflammation and the patient's functional state.[14] Low grade inflammation in atherosclerosis might be associated with oxidative stress and follow-on decrease in vit C concentration.[15] In a project conducted by Shimoni et al. it

was seen that increased anxiety could be one of the factors leading to metabolic syndrome disease in pre-diabetes patients.[16] Free radical activity and oxidative damage have been concerned in the initiation of vascular disease and antioxidants supply the first line of defense against free radicals. Several studies have shown that episodes of ischemia –reperfusion can reduce the total antioxidant capacity.[17] Project by Margarita L, et al., Serum levels of TAC had a negative significant correlation with metabolic syndrome patients with stroke with r = 0.348, P = 0.051.[18] It is probable therefore that the longer or more harsh the bouts of ischemia, increased the reduction in the total antioxidant capacity and following increase in the danger of developing infective complications. In detail it has been revealed that antioxidant defenses in pre-diabetes patients are lower than age matched controls. But these patients comprise an unimpaired nutritional status with low total antioxidant capacity, they might help from antioxidant supplementation.

Chrysohoou et al., described that obese or overweight participants had lower TAC concentrations evaluated to normal individuals.[19] Lower TAC might partially clarify their increased risk for diabetes and chronic hypertension. Uric acid was established to be elevated in both obese and metabolic syndrome patients, but significantly higher in patients with metabolic syndrome.[20] Uric acid contributes to 60% of the total antioxidants evaluated by FRAP assay, while ascorbic acid contributes 15%, protein 10%, others by 5%.

The present project shows that obesity with pre-diabetes in cases has increased levels of oxidative stress revealed 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 pro-inflammatory state of obesity and chronic pre-diabetes might also initiate due to excessive caloric intake.[21] Oxidative stress is caused by the occurrence of free radicals or radical generating agents in concentrations that overwhelm natural radical blocking or scavenging mechanisms. These free radicals react with cellular components forming products like hydroperoxides, MDA, protein carbonyl etc.[22]

Inflammatory cytokines discharged by adipocytes can also bring and worsen oxidative stress. The increased levels of oxidative stress and chronic subclinical inflammatory state seen in chronic hypertensive patients directs to higher risk of atherosclerotic and other metabolic syndrome complications. Thus, the estimation of TAC can be used as an important tool to evaluate the level of oxidative stress in obesity and chronic hypertension. The condition of elevated oxidative stress can be a potential objective for preventive and therapeutic interventions prior to advance of complications.

CONCLUSION: In the current study, it has been found that plasma fibrinogen levels are raised in pre-diabetes at the same time as the TAC has decreased. The role of plasma fibrinogen as pro-atherogenic causes has already been explained. Additional studies on a larger sample sizes with similar conclusion might evaluate plasma fibrinogen as biomarkers to forecast future metabolic syndrome and atherosclerotic changes.

Parameter	Control	Cases	P value
TAC	187.76±40.40	89.97±38.11	<0.001*
Plasma Fibrinogen	263.313±51.35	377.27±79.79	<0.001*
BMI	22.07±2.25	29.20±3.55	<0.001*

Table 1: Serum Total antioxidant Capacity, Plasma Fibrinogen levels and BMI in Pre-diabetes men and healthy controls

*Statistically significant (P value <0.001).

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