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ROLE OF ADIPONECTIN AND HS-CRP WITH GLYCEMIC CONTROL IN CORONARY ARTERY DISEASE WITH AND WITHOUT TYPE-II DIABETES MELLITUS.

Biochemistry

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ABSTRACT

Background: Atherosclerosis of the coronary arteries causes Coronary artery disease (CAD) and is the leading cause of mortality and morbidity among patients with type 2 diabetes mellitus.

Objective: To evaluate the role of adiponectin and hs-CRP in CAD with and without T2DM.

Methods: Total 120 subjects (age group 25-70 years) of either sex were enrolled. The subjects were categorized into four groups i.e. Group I (30-Controls), Group II (30-DM with CAD), Group III (30-non-diabetic with CAD) and group IV (30-DM). Adiponectin and hs-CRP were estimated by ELISA and immune-turbidimetric method respectively.

Results: The mean level of adiponectin was decreased whereas increase in level of hs-CRP in all study groups compared to controls and were significant ($p \leq 0.001$).

Conclusion: Due to alteration in the inflammatory markers in CAD, the early assessment of such markers can help to identify high risk patients.

KEYWORDS

Coronary artery disease, Adiponectin, Diabetes Mellitus.

Introduction:

Coronary artery disease (CAD) is the leading cause of mortality and morbidity among patients with type 2 diabetes. [1] Elevated cardiovascular risk is a serious complication in people with type 2 diabetes mellitus (T2DM). Indeed, approximately two-thirds of people with T2DM die of heart disease or stroke. People with diabetes often have other risk factors for cardiovascular disease (CVD), including obesity, high blood pressure and high lipid levels. [2] South Asians especially might have an underlying pro-inflammatory state that contributes to their increased risk for both T2DM and CVD. Typical Asian Indian phenotype which includes increased insulin resistance, higher waist circumference despite lower body mass index, lower adiponectin and higher high sensitive C-reactive protein (hs-CRP) makes Indians more prone to diabetes and premature CAD. Secretion of various bioactive substances from adipose tissue, conceptualized as adipocytokines, has been widely recognized to play a contributory role in insulin resistance, diabetes and CVD. In contrast to circulating inflammatory factors, adiponectin has anti-diabetic, anti-atherogenic and anti-inflammatory properties. Lower adiponectin levels were found to be associated with obesity, T2DM and CAD.[1]

Inflammation is central to the initiation and progression of atherosclerosis and to triggering CVD events.[3] Arterial inflammation plays a pivotal role in the atherosclerotic process.[1] hs-CRP is a critical component of the immune system, a complex set of proteins that our bodies make when faced with a major infection or trauma. hs- CRP levels predict recurrent coronary events among patients who already suffer from heart disease and that the prognosis of patients in the acute phase of a heart attack is tightly linked to CRP levels. However, the most important current use of CRP is in primary prevention, that is, in the detection of high risk among individuals. Individuals with elevated levels of CRP have a risk about 2 to 3 times higher than the risk of those with low levels. [4] Substantial evidence shows that low circulating adiponectin levels are associated with an increased risk of CAD. But, there are limited data available from India on the association of adiponectin and inflammatory marker hs-CRP in coronary artery disease and diabetes. [1] Hence, the present study was planned to evaluate the adiponectin & hs-CRP levels with glycemic control in CAD with & without T2DM.

Materials and Methods:

The present study was conducted in the Department of Biochemistry in collaboration with Department of Medicine and Cardiology at MGM's Medical College & Hospital, Kamote Navi Mumbai after getting approval from Institutional Ethics Committee. The study groups consist of total 120 subjects of either sex having age 25-70 years and were categorized into the following four groups.

Group-I:-30 Healthy individuals comprised Controls group.
Group-II:-30 patients with Diabetes Mellitus with coronary artery disease
Group-III:-30 Non-Diabetic Patients with coronary artery disease
Group-IV:-30 patients with Diabetes Mellitus without coronary artery disease

Inclusion criteria:

Following patients were included for the study –

- Patients with diabetes with CAD.
- Patients with diabetes without CAD.
- Non-Diabetic Patients with CAD.
- Controls from in and around MGM's Medical College and Hospital.

Exclusion criteria:

Patients with sexually transmitted disease, rheumatoid arthritis, sepsis, asthma, malignancy, renal disease, liver disease, chronic illness, malnutrition pregnant women and were excluded from the present study.

Sample collection and processing:

About 5ml blood sample was collected from each subject with all the aseptic precautions for biochemical investigations. To get serum, samples were centrifuged at 3000 rpm for 10 minutes and were kept at -70^{0}C till analysis.

Parameters measured:

Following parameters were measured:-

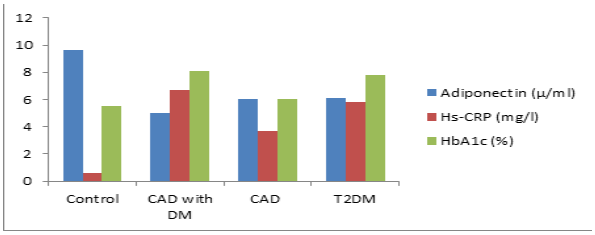
1. **Adiponectin:** Adiponectin was estimated in serum by using the quantitative sandwich enzyme immunoassay technique (assay max human adiponectin acrp 30).
2. **High sensitive C-reactive protein (hs-CRP)**: hs-CRP was estimated in serum samples using particle enhanced immune-turbidimetric method by photometric measurement of antigen–antibody reaction of antibodies to human CRP bound to polystyrene particles with CRP present in the sample.
3. **Glycated Hemoglobin (HbA1c)**: The D-10 HbA1C Program utilizes principles of ion-exchange high-performance liquid chromatography (HPLC).

Statistical analysis:
All results were analyzed by 'SPSS, Version 16' and presented as mean ± S.D. A *'p'* value of ≤ 0.05 was considered significant.

Observations and Results:
Table No. 1:- Comparison of Adiponectin, hs-CRP & HbA1c in Control Group & Study Groups

Parameters	Group-I (Control) Mean± SD	Group-II (CAD with DM) Mean± SD	Group-III (CAD) Mean± SD	Group-IV (T2DM) Mean± SD
Adiponectin (µ/ml)	9.6±1.4	5.0±1.2**	6.0±2.1**	6.1±1.8**
Hs-CRP (mg/l)	0.6±0.2	6.7±0.9**	3.7±0.6**	5.8±0.8**
HbA1c (%)	5.5±0.4	8.1±1.0**	6.0±0.6**	7.8±0.8**

Figure: - 1



Discussion:
The role of inflammation in the pathogenesis of atherosclerosis has been firmly established in the past two decades. Numerous studies, both observational and randomized controlled trials (RCTs) have shown an association of pro-inflammatory biomarkers with incidence of hypertension, metabolic syndrome, CAD and ACS. Adiponectin, as an insulin sensitizer can effectively enhance glucose uptake and lipid metabolism and it is a recently introduced inflammatory cytokine and some studies revealed its important metabolic effects.[5,6,7]

The mean serum level of adiponectin was decreased in all study groups as compared to controls and was statistically highly significant ($p \leq 0.001$). Our results are in consistent with the study conducted by Hotta *et al.,* who showed significant lower plasma adiponectin levels in patients with type 2 diabetes and CAD, than in patients with diabetes without CAD.[8] Kumada *et al.,* reported that hypoadiponectinaemia (<4µg/ml) was independently associated with the presence of CAD after adjustment for other well-known CAD risk factors in men.[9] Similarly, Satyavani *et al.,* found that adiponectin levels were significantly lower in subject with either diabetes or CAD and much lower in subject who had both as compared to control subjects.[1] Mohan *et al*., reported that lower adiponectin levels were associated with the metabolic syndrome and its components, particularly, diabetes and dyslipidaemia in Asian Indians, a high risk group for premature CAD and diabetes. Therefore, it is likely that adiponectin could be beneficial and high levels of circulating adiponectin would confer vascular protection; it inhibits TNF-α stimulated expression of adhesion molecules on endothelial cells and prevents the development of atherosclerosis. Thus, adiponectin may function as a therapeutic target for diabetic patients with and without CAD.[10] In our study, the mean value of hs-CRP was significantly increased in all the study groups ($p \leq 0.001$) as compared to controls. The results of our studies are supported by Guruprasad *et al.,* who found that elevated levels of hs-CRP in patients with ACS as compared to controls and positive association with CAD.[11] Our findings also support by Ridker *et al.,* who showed that reduced levels of hs-CRP results in decreased incidence of cardiovascular events.[12]

Similarly for HbA1c, Table 4 shows the mean values of HbA1c were significantly high in group II & IV as compared to control group ($P \leq 0.001$); that suggest there is poor glycemic control but in group III although it is with in normal range ($P \leq 0.05$). Such outcomes emphasize the need to lower the HbA1c in our patients to avoid long-term complications and reduce the burden of economic costs as well as provide a better quality of life for patients. HbA1c has been the key measure of glycemic control in diabetic patients for last two decades. It is considered to be the gold standard marker, and most widely accepted test of glycaemia among clinicians and patients.

Conclusion:
The current study highlighted that subjects with CAD had lower adiponectin level and elevated level of hs-CRP. An adiponectin level was also decreased in subjects with diabetes as reported in cardiovascular risk factor. The results of present study indicate that there occurs alteration in inflammatory markers in CAD. Hence, early assessment of such markers can help to identify high risk patients. However, further studies with adequate sample size are warranted to finally accept the concept.

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