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The association of lipid profile and Cyclophilin A in diabetic patients with coronary artery disease.

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ABSTRACT
Background: Cyclophilin A (CypA) can be utilized as an early predictor of CAD and lipid profile are one of the markers to detect the CAD. Study aimed to assess the association between the lipid profile and Cyp A among the diabetic patients with coronary artery disease.
Material & Method: Between November 2017 and May 2019, all patients enrolled in the cardiac department at PMSSY Bangalore Medical College were included in the study. The current study recruited people with a known history of diabetes mellitus for 5-10 years who were willing to participate in the trial and was above the age of 40. The patients were separated into two groups: Group A, which comprised diabetics with CAD as cases, and Group B, which included diabetics without CAD as controls. Lipid profile, Cyp-A, and HBA1c levels were measured in blood samples.
Result: A total of 71 patients were involved in the current study, with 36 in group A and 35 in group B. The male to female ratio was 2:1, with 39 percent being female and 61 percent being male individuals. Total cholesterol and LDL-cholesterol levels differed significantly between the two groups. There was a significant strength of correlation between serum cholesterol and serum LDL with Cyp-A among patients, as well as a significant negative association with serum HDL.
Conclusion: Cyp-A levels are increased in patients with CAD patients with DM. There is a significant positive association between the Cyp-A with the serum cholesterol, LDL and negative association with the HDL cholesterol.
Keywords: Cyclophilin A, Coronary Artery Disease, Cholesterol, HbA1c, HDL, LDL.

I. INTRODUCTION

Coronary artery disease is a complicated chronic inflammatory illness marked by remodeling and constriction of the coronary arteries that deliver oxygen to the heart. It is the biggest cause of mortality worldwide, accounting for around one-third of all deaths in people over the age of 35. Cyclophilin A (CyPA) is a protein that vascular smooth muscle cells (VSMCs) release in response to reactive oxygen species (ROS). CyPA is thought to play a key role in the final stages of atherosclerosis and plaque rupture. However, little research had been done on the potential link between CyPA and CAD.[1]

Cyclophilin A (CypA) can be utilized as an early predictor of CAD and to distinguish between those with zero-vessel disease and those who are healthy. The combination of hypertension as a risk factor with high CyPA levels improves diagnostic sensitivity and specificity. Study aimed to assess the association between the lipid profile and Cyp A among the diabetic patients with coronary artery disease.

II. MATERIAL & METHOD

The study covered all patients enrolled to the cardiac department at PMSSY Bangalore Medical College between November 2017 and May 2019. The patients having known history of diabetes mellitus for 5-10yrs of duration and willing to take part of study with age >40 were included in present study. The patients were divided into two groups: Group A, which included diabetes mellitus patients with CAD as cases, and Group B, which included diabetes mellitus patients without CAD as controls. Diabetes was diagnosed by measuring HbA1c and/or fasting blood sugar (FBS) levels in accordance with ADA guidelines.[2] Already diagnosed cases of CAD with Type2 Diabetes from Cardiology was taken as cases (positive treadmill test in accordance with American Heart Association). Type 2 Diabetes patients diagnosed with no CAD was taken as controls by similar criteria.

Fasting blood samples of 5mL were taken from patients and controls in EDTA and plain vacutainers. Samples were allowed to clot for 2 hours at room temperature before centrifugation for 15 minutes at 1000g at 28 C for Cyclophilin A

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level by sandwich immunoassay kit, Cyclophilin A was measured by latex enhanced immunoturbidimetry method, and HBA1c by BioRad D-10 analyser, which employs principles of ion-exchange high-performance liquid chromatography (HPLC).

Statistical analysis: All data was entered into an excel spreadsheet and analyzed with the window-based SPSS v21. For data that is not normally distributed, the data is expressed as a mean standard deviation; the median and inter-quartile ranges are shown. The mean difference between normally distributed data and non-normally distributed data was calculated using the student t-test and the Mann-Whitney U test. A statistically significant p-value of 0.05 was considered.

III. RESULT:

The current study included 71 patients, who were divided into two groups: Group A: As instances, 36 Type 2 diabetic patients with Coronary Artery Disease (CAD) were identified. (TMT is positive.)

Group B: 35 age and gender matched type 2 diabetes mellitus patients with no coronary artery disease (CAD) served as controls. (TMT is negative.)

In the current study, 39 percent of the subjects were female and 61 percent were male, with a male to female ratio of 2:1. Among the 71 individuals included, 36 had coronary angiography performed, whereas the remaining 35 were neither required nor advised for angiography. (Table No 1)

Table 1: Mean age of the patients in two groups.

	Group A Mean ± SD	Group B Mean ± SD	p-value
Age in Years	58.5 ± 10.47	57.6 ± 9.47	.69
p-value <.05 statistically significant. Group A: DM with CAD; Group B: DM without CAD.			

Table 2: Demographic details of the study subjects.

	Group A (DM with CAD)		Group B (DM without CAD)		
	Mean	Standard Deviation	Mean	Standard Deviation	p-value
Height in cms	163.89	7.78	160.65	9.41	.117
weight in Kgs	65.35	10.06	61.18	10.15	<.05
BMI	24.21	2.43	23.59	2.40	.284
Pulse rate per min	84.59	5.35	84.12	5.97	.724
Systolic Blood pressure	147.30	18.36	139.41	16.13	<.05
Diastolic Blood Pressure	104.32	15.91	97.35	14.83	<.05
Fasting Blood Sugar mg/dL	208.51	73.62	190.76	76.02	.321
Duration of Diabetes Mellitus	7.59	2.05	7.15	2.05	.361
HbA1c %	10	3	9	2	.712
P<.05 statistically significant; <.001 statistically highly significant.					

There was no significant difference in the mean levels of HbA1c levels and duration of diabetes mellitus in both the groups. There was a significant mean difference of weight and blood pressure among both the groups. (Table No 2)

Table 3: Showing the median value of hs-CRP and Cyclophilin A in both groups using Mann-Whitney U Test.

Mann-Whitney U Test	Group A (DM with CAD) Median (Minimum – maximum)	Group B (DM without CAD) Median (Minimum – maximum)	p-value
Cyclophilin A (ng/ml)	13.3 (1.44-60.06)	8.71 (0.5-31.6)	.001**
P<.05 statistically significant; <.001 statistically highly significant.			

In present study, there is a significant higher mean of plasma Cyp A among group A patients, compared to the group B patients. (Table No 3)

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Table 4: Mean difference in Lipid profile among Group A (DM with CAD) and Group B (DM without CAD)					
	Group A (DM with CAD)		Group B (DM without CAD)		
	Mean	Standard Deviation	Mean	Standard Deviation	p-value
Total Cholesterol in mg/dL	264.51	60.10	218.06	53.71	.001**
High Density Lipoprotein in mg/dL	47.11	54.48	43.53	12.37	.710
Very low density lipoprotein in mg/dL	40.38	25.21	41.12	22.26	.897
Low density lipoprotein in mg/dL	184.57	35.47	133.82	38.50	.001**
Triglycerides in mg/dL	192.70	119.21	198.06	107.28	.843
Urea in mg/dL	31.73	13.18	29.88	15.56	.590
Creatinine in mg/dL	1.12	.88	.88	.42	.143
P<.05 statistically significant; <.001 statistically highly significant.					

Among the lipid profile results, the total cholesterol and LDL-cholesterol showed a significant mean difference in two groups. (Table No 4)

Table 5: Showing the correlation of hsCRP with lipid profile in the patients		
		Cyclophilin A (ng/ml)
Total Cholesterol in mg/dL	r	.677
	Sig	.01*
High Density Lipoprotein in mg/dL	r	-.228
	Sig	.05*
Very low density lipoprotein in mg/dL	r	.356
	Sig	.33
Low density lipoprotein in mg/dL	r	.186
	Sig	.03*
Triglycerides in mg/dL	r	.143
	Sig	.907
P<.05 statistically significant; <.001 statistically highly significant.		

There is a significant positive strength of association between the serum cholesterol and the serum LDL with the Cyclophilin A among patients. There was significant negative association with the serum HDL. (Table No 5)

IV. DISCUSSION:

Atherosclerosis of the coronary arteries of the heart causes CAD.[3] Complications involving susceptible atherosclerotic plaque are caused by two key mechanisms: dyslipidemia and inflammation, both of which are impacted by traditional risk factors. Each mechanism provides extra data on cardiovascular events and mortality.[4]Abnormal lipid profile is seen among the patients with the CAD. The elevated level of serum cholesterol, LDL and decrease level of HDL, with elevated levels of the atherosclerosis risk indices are seen in patients with the coronary artery disease patients.[5,6]

Plasma In reaction to oxidative stress and inflammation, monocytes and vascular wall cells release CypA, but it can also be secreted or leaked by injured cardiomyocytes and interstial fibroblasts. Oxidative stress and vascular damage both increased CypA expression and release. The first is to identify CypA as a secreted redox-sensitive mediator, the second is to establish CypA as a vascular smooth muscle cell growth factor, and the third is to propose a significant involvement in the etiology of vascular disease.[4,4,7]

Plasma Cyclophilin A (CypA) was found to be significantly higher in Group-1 patients [13.3 (1.44 – 60.06)] compared to patients in Group-2 [8.71 (0.5 – 31.6)] (p-value <.001). Study conducted by Yan et.al, also found that patients with ACD or ACS was significantly higher than those with controls and stable angina. The increased levels of CypA may be a valuable marker for predicting the severity of acute coronary

disease.[8] in concordance, study conducted by Satoh et.al., reported that plasma CypA levels were significantly higher in DM patients with coronary disease than DM patients without CAD.[9]

There is a significant positive strength of association between the serum cholesterol and the serum LDL with the Cyclophilin A among patients. There was significant negative association with the serum HDL. In similar to presents study, Alfonso A et al., found a significant correlation between the atherosclerosis and CypA among the patients.[10]

Conclusion: Cyp-A levels are increased in patients with CAD patients with DM. There is a significant positive association between the Cyp-A with the serum cholesterol, LDL and negative association with the HDL cholesterol.

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