Original Research Paper

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Biochemistry

"CYCLOPHILIN A AS AN IMPORTANT INFLAMMATORY RISK MARKER OF CAD IN DIABETES MELLITUS PATIENTS"

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ABSTRACT

Background: Cyclophilin A is part of various intracellular functions, such as intracellular signaling, protein trafficking, and regulating activity of other proteins.(1) The secretory nature of Cyclophilin A (CypA) and its presence in the plasma of the patients with diabetes mellitus and coronary artery disease (CAD) are important potential biomarkers for the disease. This study aimed to assess the Cyclophilin A among the patients with diabetes mellitus with coronary artery disease and without coronary artery disease in them

Material And Method: All the patients admitted under cardiology department of PMSSY Bangalore medical college were included in present case control study, conducted between November 2017 to May 2019. The patients with known history of diabetes mellitus for 5-10yrs of duration and willing to be part of study with age >40 were included in present study. The patients were grouped as Group A with diabetes mellitus patients having CAD as cases and group B patients were diabetes mellitus patients without CAD as controls.

Result: Total of 71 patients were included, among them 37 were in group A and 34 were in group B. There was a significant higher median levels of Cyclophilin A among the diabetes mellitus patients with CAD [13.3 (1.44 – 60.06)ng/ml] compared to diabetics without CAD [8.71 (0.5 – 31.6)ng/ml]. There was a significant strength of association between the HbA1c and the plasma CypA levels among the patients.

Conclusion: Cyclophilin A has a potential role in promoting vascular disease in diabetic patients and reveled that CypA is a good biomarker for CAD.

KEYWORDS : Diabetes mellitus, coronary artery disease, Cyclophilin A, HbA1c.

INTRODUCTION

Diabetes mellitus (DM) is associated with multisystem complications such as microvascular disorders such as retinopathy, nephropathy and neuropathy and often associated with macrovascular risk such as ischemic heart failure, stroke and peripheral artery disease. Cyclophilin A is part of a variety of intracellular activities, such as intracellular signalling, protein trafficking and the regulation of other protein production.[1] The secretive nature of Cyclophilin A (CypA) and its plasma expression in patients with diabetes mellitus and coronary artery disease (CAD) are significant possible biomarkers of the disease. It is secreted by monocytes in response to hyperglycemia, acting as a possible marker in type 2 DM.[2]

This study aimed to assess the Cyclophilin A among the patients with diabetes mellitus with coronary artery disease and without coronary artery disease in them.

MATERIAL & METHOD

All the patients admitted under cardiology department of PMSSY Bangalore medical college were included in present case control study, conducted between November 2017 to May 2019. The patients with known history of diabetes mellitus for 5-10yrs of duration and willing to be part of study with age >40 were included in present study. The patients were grouped as Group A with diabetes mellitus patients having CAD as cases and group B patients were diabetes mellitus patients without CAD as controls. Diabetes was assessed by recording HbA1c and/or fasting blood sugar (FBS) levels in accordance to ADA criteria[3] 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.

5mL of fasting blood samples was collected from the cases and controls in EDTA and plain vacutainers. Samples allowed to clot for 2 hours at room temperature before centrifugation for 15 min at 1000×g at 2~8˚ C but for HbA1c without centrifugation and analyzed for Cyclophilin A level by sandwich immunoassay kit, HBA1c by BioRad D-10 analyser utilizes principles of ion-exchange high-performance liquid chromatography (HPLC).

Statistical Analysis:

All the data was entered in excel sheet and analysed using SPSS v21 operating on windows. The data are represented as mean standard deviation, for data not normally distributed, median and inter-quartile range was mentioned.

The mean difference between the normally distributed data was analysed using student t-test and the data not-normally distributed used the Mann-Whitney U Test. a p-value of <0.05 was considered statistically significant.

RESULTS

Total of 71 patients were included in the present study, grouped into, Group A: 37 already diagnosed Type 2 diabetic patients with Coronary arterial disease (CAD) as cases. (TMT positive).

Group B: 34 age and sex matched patients of type 2 diabetes mellitus without Coronary arterial disease (CAD) as controls. (TMT negative).

In present study, 39.4% were female and 60.6% are male subjects, with male to female ratio of 2:1. Among 71 patients included, 37 underwent Coronary angiography and other 34 did not required / indicated for angiography.

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 ± 9.47	58.2 ± 10.47	.69
p-value <.05 statistically significant. Group A: DM with CAD; Group B: DM without CAD.			

The mean age between the groups was not significantly different. No history of weight gain by patient in last few months.

Table 2: Showing the median value of 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
P. 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.			

Table 3: 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)		p-value
	Mean	Standard Deviation	Mean	Standard Deviation	
Total Cholesterol in mg/dL	164.51	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	84.57	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.					

Table 4: Correlation of Cyclophilin A and HbA1c levels.

		Plasma Cyclophilin A ng/mL
HbA1c %	r	.504**

r- Pearson's correlation. *. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.001 level (2-tailed).

DISCUSSION

Plasma CypA is secreted by monocytes and vascular wall cells in response to inflammation and oxidative stress, but can also be secreted by or leaked from damaged cardiomyocytes and interstial fibroblasts. CypA expression and secretion increased by oxidative stress and vascular injury. They are the first to recognise CypA as a secreted redox-sensitive mediator, to establish CypA as a vascular smooth cell growth factor and to indicate a significant function in vascular disease pathogenesis.[4]

CAD occurs due to atherosclerosis of the coronary arteries of the heart. Complications involving the vulnerable atherosclerotic plaque are triggered by two major mechanisms, dyslipidemia and inflammation, although both are influenced by classic risk factors. Each mechanism provides additional information regarding the cardiovascular events and mortality. [4]

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). A study performed by Yan et.al also showed that patients with ACD or ACS were considerably higher than those with regulated and stable angina. Increased levels of CypA can be a helpful indicator for predicting the risk of acute coronary disease.[5] Concordance, a study performed by Satoh et al. found that plasma CypA levels were substantially higher in DM patients with coronary artery disease than in DM patients without CAD.[6] Also glucose and HbA1c were positively associated with plasma CypA levels (r=0.504; p<.05) indicating a specific relation of plasma CypA levels with Hyperglycemia.

CONCLUSION:

This study demonstrated that CypA has a potential role in promoting vascular disease in diabetic patients and revealed that CypA is a good biomarker for CAD. But combining CyPA levels with other biomarker hs-CRP would further improve the prognostic impacts for patients with CAD. However further studies need to be done to substantiate this findings.

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REFERENCES

1. Satoh K, Shimokawa H, Berk BC. Cyclophilin A: promising new target in cardiovascular therapy. Circ J. 2010/10/15. 2010;74(11):2249–56.
2. Ramachandran S, Venugopal A, Sathisha K, Reshmi G, Charles S, Divya G, et al. Proteomic profiling of high glucose primed monocytes identifies cyclophilin A as a potential secretory marker of inflammation in type 2 diabetes. Proteomics. 2012;12(18):2808–21.
3. Association AD. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010;33 Suppl 1(Suppl 1):S62–9.
4. Jin ZG, Melaragno MG, Liao DF, Yan C, Haendeler J, Suh YA, et al. Cyclophilin A is a secreted growth factor induced by oxidative stress. Circ Res. 2000;87(9):789–96.
5. Yan J, Zang X, Chen R, Yuan W, Gong J, Wang C. The clinical implications of increased cyclophilin A levels in patients with acute coronary syndrome. Clin Chim Acta. 2012;2012:691–5.
6. Satoh K, Nigro P, Berk BC. Oxidative Stress and Vascular Smooth Muscle Cell Growth: A Mechanistic Linkage by Cyclophilin A. Antioxid Redox Signal. 2010;12(5):675–82.