Original Research Article

Serum PON-1 activity in the diabetes mellitus patients for predicting the atherogenic risk

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Abstract

Background: PON-1 activity has been demonstrated to be inversely related to the risk of cardiovascular disease and a reduction in PON-1 activity has been reported in states of high oxidative stress such as uncontrolled diabetes. Thus, estimation of serum PON-1 activity in diabetes mellitus is being valuable in predicting atherosclerosis and future cardiovascular events. **Aim:** To evaluate the serum PON-1 activity in diabetes mellitus for predicting atherogenic risk. **Material and Methods:** A total of 100 subjects were included in the present study. Out of this 100, 50 were study group (patients with DM) and the other 50 were control group (healthy individuals).PON-1 activity was estimated using the paraoxon (O,O diethyl-O-4 nitrophenyl phosphate) as the substrate for hydrolysis. The chemicals used were of analytical reagent grade from Sigma chemicals. Glucose, urea, creatinine, total cholesterol, HDL cholesterol and Triacylglycerol were estimated. **Results:** The serum PON-1 activity between the control (270.50±81.11) and study groups (99.19±38.71). There is a highly significant difference between the two groups (p=<0.0001).Both HDL and PON activity are significantly decreased in the study group. **Conclusion:** PON-1 activity may act as a useful marker for early prediction of atherosclerosis in DM. By predicting earlier, early interventional measures by pharmaceutical means or by dietary means can be done.

Key Words: Diabetes mellitus, paraoxanase-1activity, atherosclerosis, marker.

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INTRODUCTION

Diabetes Mellitus (DM) is characterized by increased oxidative stress and considered as a major risk factor for the development of atherosclerosis and coronary artery disease (CAD) despite current treatments for DM.[1] Moreover, methods to assess CAD risk adequately in asymptomatic individuals are not yet available.[2]Atherosclerosis and its complications accounts for about 80% of mortality in diabetes mellitus. Human paraoxonase 1 (PON1), which has PON, arylesterase (ARE), and diazoxonase activities, is a calcium-dependent ester hydrolase exclusively bound to the serum high-density lipoprotein (HDL).[3] It has antioxidant and anti-atherogenic properties and enables protection of both low-density lipoproteins (LDLs) and HDLs against lipid peroxidation.[4,5] PON1 activity has been demonstrated to be inversely related to the risk of cardiovascular disease,[6] and a reduction in PON1 activity has been reported in states of high oxidative stress such as uncontrolled diabetes.[7] Thus, estimation of serum PON-1 activity in diabetes mellitus is being valuable in predicting atherosclerosis and future cardiovascular events. Therefore, the present study was conducted to evaluate the serum PON-1 activity in diabetes mellitus for predicting atherogenic risk.

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MATERIAL AND METHODS

The study included 100 subjects in the age group of 21-72 years from both sexes. Approval from Institutional Ethical Committee was obtained prior to the study and an informed consent was obtained from all the included subjects. The study population includes 2 groups: i. Control group - consists of 50 healthy individuals (25 females and 25 males) and ii. Study group - consists of 50 patients with DM (25 females and 25 males).In the study group, both type1 and typeII DM patients, with duration of diabetes from 1to15 years were included. 17 patients were under insulin and 33 were under oral hypoglycemic drugs. Patients with liver diseases, renal failure, acute and chronic infections, chronic inflammatory disorders, thyroid disorders, hypertension, known smokers, alcoholic and on lipid lowering drugs and anti-oxidants were excluded from the study.

Sample Collection: Under aseptic precautions, fasting venous blood sample of 6ml was collected from each subject.2 ml of collected blood was transferred to a plain tubes and 2ml of blood to a EDTA containing vacutainers and 2 ml to fluoridated tubes. 10 µl of whole blood from EDT A tubes added to 500 µ l of haemolysing reagent and lysate prepared for HbA1c estimation. The vacutainers containing the blood samples were kept at room temperature for 30 min and were centrifuged at 2000 g for 15 minutes for clear separation of serum. Paraoxonase activity, glucose, urea, creatinine, total cholesterol, HDL cholesterol and Triacyl glycerol were estimated immediately after the serum was separated. LDL and VLDL cholesterol levels were calculated from the estimated parameters. 2 ml of post prandial venous blood sample was collected in fluoridated tubes for the estimation of post prandial blood glucose level.

Measurement of PON-1 Activity: PON-1 activity was estimated using the paraoxon (O,O diethyl-O-4 nitrophenyl phosphate) as the substrate for hydrolysis. The chemicals used were of analytical reagent grade from Sigma chemicals.

RESULTS

A total of 100 subjects were included in the present study. Out of this 100, 50 were under the study group (patients with DM) and the other 50 were under the control group (healthy individuals).25 Male and 25 female subjects in control and study group in the age group of 21-72 years were included in this study. The mean age of the control group was 47.4±12.01years and for the study group was 47.5 ±13.45years. The two groups were found to be age matched and sex matched.

Table 1: Comparison of PON-activity between control and study group

S.N.	PON activity (IU/L)	Mean	S.D.	Statistical inference
1	Control (n=50)	270.5084	81.11600	p=0.0001 < 0.05 (Significant)
2	Study (n=50)	99.1958	38.71695	

The serum PON1 activity between the control (270.50±81.11) and study groups(99.19±38.71). There is a highly significant difference between the two groups (p=<0.0001).

Table 2: Comparison of all parameters between control and study group

S.N.	Factors	Mean	S.D	Statistical inference
			PONACT (IU/L)	
1	Control (n=50)	270.5084	81.11600	p=0.0001 (<0.05 Significant)
	Study (n=50)	99.1958	38.71695	
			FBS	
2	Control (n=50)	80.6200	10.81173	p=0.0001 (<0.05 Significant)
	Study (n=50)	158.4000	50.96257	
			PPBS	
3	Control (n=50)	121.8400	10.78048	p=0.0001 (<0.05 Significant)
	Study (n=50)	262.9800	72.50067	
			HbA1c%	
4	Control (n=50)	4.6120	.52085	p=0.0001 (<0.05 Significant)
	Study (n=50)	7.2980	1.07864	
			CHOL	
5	Control (n=50)	149.6600	8.00411	p=0.0001 (<0.05 Significant)
	Study (n=50)	205.9400	26.11936	
			TGL	
6	Control (n=50)	109.94	15.676	p=0.0001 (<0.05 Significant)
	Study (n=50)	189.88	21.167	
			HDL	
7	Control (n=50)	44.2400	2.12430	p=0.0001 (<0.05 Significant)
	Study (n=50)	35.2800	3.86000	
			LDL	
8	Control (n=50)	83.4320	8.86924	p=0.0001 (<0.05 Significant)
	Study (n=50)	132.6840	24.74415	
			VLDL	
9	Control (n=50)	21.9880	3.13516	p=0.0001 (<0.05 Significant)
	Study (n=50)	37.9760	4.23333	

There was highly significant difference observed between the study and control group in all the parameters (p=<0.0001) (Table 2).

DISCUSSION

Atherosclerotic macrovascular complication (especially coronary artery disease) is the leading cause of morbidity and mortality in DM.[1] Paraoxonase-1(PON-1) is an enzyme that confers the antiatherogenic and antioxidant properties to HDL. PON-1 activity is responsible for the antiatherogenic property of HDL. By measuring the PON-1 activity in DM patients, we can predict the atherosclerosis earlier, and it may help for taking early

preventive measures against cardiovascular disease. Comparison of mean value of the serum PON-1 activity in the study group (99.19 ± 38.17 U/L) with that of the control group (270.50 ± 81.11) showed a significant fall in the study group (P= <0.0001). This study also supports the fact that there is a significant decrease in PON-1 activity in DM.[7,8]A study results by Amine *et al* showed an important reduction of the PON1 activity in diabetic patients compared to the healthy group.[9] These results were supported by Rosenblat *et al.*[10] Our study also showed decreased PON1 activity in diabetic patients. Besides the changes in lipid parameters, metabolic abnormalities observed in DM affect the reduction of the antioxidant capacity of HDL, and also the decreasing PON1 activity via changes in the activity of lipoprotein lipase leading to accelerate atherosclerosis process.[11] The difference in the level of lipid parameters, between the two groups are associated with dyslipidemic changes in the diabetes mellitus. Among the other parameters measured, fasting blood sugar, post prandial blood sugar and HbA1C levels are significantly increased in the study group with the P-value of <0.0001 indicating the presence of uncontrolled hyperglycemia in the study group. In the Pearson's correlation analysis, the PON activity shows highly significant negative correlation with age in years (P= <0.01). It shows a possible relation between PON activity and age and PON activity diminishing with duration of DM, could be a non-negligible factor of increased atherosclerosis development in elderly people with DM.[12] The levels of HDL shows a significant positive correlation with the PON activity (P= <0.01). This correlation proves the association of PON with HDL. Both HDL and PON activity are significantly decreased in the study group.

CONCLUSION

PON-1 activity may act as a useful marker for early prediction of atherosclerosis in DM. By predicting earlier, early interventional measures by pharmaceutical means or by dietary means can be done.

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