

# Correlation between serum PON-1 activity and lipid profile in diabetes mellitus

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## Abstract

**Background:** PON1 has detoxification activity in atherosclerotic processes. Serum PON1 activity has been shown to be reduced in atherogenesis. Thus, estimation of PON activity in diabetes mellitus is being valuable in predicting atherosclerosis and future cardiovascular events. **Aim:** To correlate serum PON-1 activity and lipid profile in diabetes mellitus. **Material and Methods:** A total of 100 subjects were selected and were grouped into: Control group (50 healthy individuals) and Study group (50 patients with diabetes mellitus). Serum PON-1 activity and serum Glucose, Total cholesterol and HDL cholesterol were estimated. **Results:** Mean values of HDL in study group ( $35.28 \pm 3.8$ ) was significantly decreased than that of control group ( $44.24 \pm 2.12$ ). ( $P = <0.0001$ ). Comparison of mean values of lipid profile levels in control group showed a significant increase of all the above parameters in the study group ( $p = <0.0001$ ). **Conclusion:** A significant decrease in PON-1 activity was observed in DM patients. The levels of HDL shows a significant positive correlation with the PON activity. Thus, PON-1 activity may act as a useful marker for early prediction of atherosclerosis in DM.

**Key Words:** Diabetes mellitus, PON-1 activity, lipid profile, atherosclerosis.

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## INTRODUCTION

The prevalence of Diabetes mellitus is increasing worldwide and at present over 285 million people are living with diabetes across the world. For people with both type 1 and type 2 diabetes mellitus the risk of premature death due to atherosclerosis is considerable. Atherosclerosis and its complications accounts for about 80% of mortality in diabetes mellitus. Abnormalities in plasma lipoprotein concentration are commonly observed in diabetic individuals which contribute to the

atherosclerotic process.<sup>3</sup> Abnormalities of lipoproteins are responsible for increased incidence of microvascular and macrovascular complications in CHD.<sup>1</sup> Human serum paraoxonase 1 (PON1) is an HDL-C-bound enzyme and considered to be the major determinant of the antioxidant action of HDL-C (8). PON1 and HDL protect against LDL oxidative modification.<sup>2</sup> PON1 has detoxification activity in atherosclerotic processes.<sup>3</sup> Serum PON1 activity has been shown to be reduced in familial hypercholesterolemia and diseases associated with accelerated atherogenesis.<sup>4</sup> Thus, estimation of PON activity in diabetes mellitus is being valuable in predicting atherosclerosis and future cardiovascular events.

## MATERIAL AND METHODS

In this prospective study, a total of 100 subjects were selected and were grouped into two groups.

Group I: Control group included of 50 healthy individuals (25 females and 25 males) and

Group II: Study group included of 50 patients with diabetes mellitus (25 females and 25 males).

In the study group, both type I and type II diabetes mellitus patients, with duration of diabetes from 1 to 15 years were included. 17 patients were under insulin and 33 were under oral hypoglycemic drugs. Individuals with liver diseases, renal failure, acute and chronic infections, chronic inflammatory disorders, thyroid disorders, hypertension, history of smoking, alcoholism and patients on lipid lowering drugs and anti-oxidants were excluded from the study. Blood samples were collected after overnight fast from both cases and controls. Fasting blood samples were analysed for paraoxonase-1 activity, fasting blood glucose, HbA1c and lipid profile (Total cholesterol, Triglycerides, HDL, VLDL); 2 mL of post-prandial venous blood sample was collected for the estimation of post-prandial blood glucose level. Paraoxonase 1 activity was determined using paraoxon as the substrate and measured by increases in the absorbance at 405 nm due to the formation of 4-nitrophenol as previously described (8). The activity was measured at 25 °C by adding 50 µl of serum to 1 ml of Tris-HCl buffer (100 mM at pH 8.0) containing 2 mM CaCl<sub>2</sub> and 5 mM paraoxon. The rate of generation of 4-nitrophenol was determined at 405 nm. Serum Glucose, Total cholesterol and HDL cholesterol were estimated in fully automated analyser (Beckmann Coulter AU-480) using respective kits. Serum LDL cholesterol level was calculated from the estimated parameters using Friedewald's formula and VLDL from the formula TGL/5.

## RESULTS

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). The fasting blood sugar, post prandial blood sugar and Hb A1c 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.

**Table 1: Comparison of Sugar parameters and PON-1 activity**

Parameter	Control group (n=50)	Study group (n=50)	Significance
PON-1 activity	270.5084 ± 81.116	99.1958 ± 38.716	p < 0.05 Significant
FBS	80.6200 ± 10.81173	158.4000 ± 50.96257	p < 0.05 Significant
PPBS	121.8400 ± 10.78048	262.9800 ± 72.50067	p < 0.05 Significant
HBA1c%	4.6120 ± 5.2085	7.2980 ± 1.07864	p < 0.05 Significant

Analysis of parameters of lipid profile shows, that the mean values of HDL in study group (35.28 ± 3.8) is significantly decreased than that of control group (44.24 ± 2.12) (p = < 0.0001). Comparison of mean values

of Total cholesterol (205.94 ± 26.11), Triglycerides (189.88 ± 21.16), LDL (132.68 ± 24.74) and VLDL (37.97 ± 4.23) of the study group, with the mean values of total cholesterol (149.66 ± 8.00), Triglyceride (109.94 ± 15.67), LDL (83.43 ± 8.8) and VLDL (21.98 ± 3.13) of the control group showed a significant increase of all the above parameters in the study group (p = < 0.0001). 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.

**Table 2: Comparison of Lipid profile and PON-1 activity**

Parameter	Control group (n=50)	Study group (n=50)	Significance
PON-1 activity	270.5084 ± 81.116	99.1958 ± 38.716	p < 0.05 Significant
Total Cholesterol	149.6600 ± 8.00411	205.9400 ± 26.11936	p < 0.05 Significant
Triglyceride	109.94 ± 15.676	189.88 ± 21.167	p < 0.05 Significant
HDL	44.2400 ± 2.12430	35.2800 ± 3.8600	p < 0.05 Significant
LDL	83.4320 ± 8.86924	132.6840 ± 24.74415	p < 0.05 Significant
VLDL	21.9880 ± 3.13516	37.9760 ± 4.23333	p < 0.05 Significant

## DISCUSSION

PON-1 is an HDL associated antioxidant enzyme, which diminishes the LDL oxidation and prevents the pro-inflammatory response elicited by oxidised LDL, by hydrolysing the lipid peroxides.<sup>5,6</sup> Moreover PON-1 is critical, for preventing the oxidation of HDL, allowing it to maintain its function. 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). Various studies show that serum PON1 activity has been found to be significantly decreased in type 1 and type 2 diabetes compared to the healthy control subjects.<sup>7-9</sup> The protective effect of PON1 against lipid peroxidation may be decreased in diabetic patients because of the lower enzyme activity. A study by Inoue has shown decreased PON1 activities in patients with Type 2 Diabetes Mellitus though the concentration of the enzyme remains the same.<sup>10</sup> Jamuna Rani *et al* observed a significant decrease in PON1 activity with the increase in duration of Diabetes Mellitus.<sup>11</sup> Increased levels of Fasting Plasma Glucose in the Diabetic group indicate a poor glycemic control in these patients. This in turn leads to the increased glycation of proteins and other biomolecules. Prolonged hyperglycemia in these patients might have caused

increased free radical synthesis depleting the total antioxidant stores.<sup>12</sup> 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. In a study conducted by Suvarna *et al* report that the levels of HDL-C and PON1 activity are decreased significantly in diabetic patients with complications in comparison to diabetics without complications.<sup>13</sup> Singh *et al* found decreased PON1 activity in diabetic population comparison to healthy population.<sup>14</sup>

## CONCLUSION

A significant decrease in PON-1 activity was observed in DM patients. This may play an important role in causation of premature atherosclerosis. Thus, PON-1 activity may act as a useful marker for early prediction of atherosclerosis in DM.

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