

**CORRELATION BETWEEN SERUM PARAOXONASE ACTIVITY AND HIGH DENSITY LIPOPROTEIN LEVELS IN TYPE2 DIABETES PREDISPOSING TO ATHEROSCLEROSIS**<sup>1</sup>Dr.SK.Deepthi and <sup>2</sup>Dr.G.Amar Raghu Narayan,<sup>1</sup>Department of Biochemistry, Naryana Medical College, Nellore.<sup>2</sup>Department of Plastic surgery, Narayana Medical College, Nellore.

**ABSTRACT:** Human serum paraoxonase is physically associated with HDL and has been implicated in the detoxification of organophosphates and possibly in the prevention of LDL lipid peroxidation and therefore retards atherosclerosis. HDL levels are inversely related to the risk of developing atherosclerosis. We investigated the serum activity and concentration of paraoxonase and HDL levels in 104 subjects (42 diabetic patients without complications, 42 controls, 20 diabetic patients with complications.). Paraoxonase activity was found to be lower in diabetic patients than in controls. Similarly there was reduction in HDL levels in cases suggesting a positive correlation between HDL and paraoxonase levels.

**Key words:** Type2 diabetes mellitus (Type2 DM), High density lipoproteins (HDL), Paraoxonase (PON1), Fasting Glucose (FSG), Atherosclerosis, Low-density lipoproteins (LDL)

**INTRODUCTION**

Diabetes mellitus is a chronic disorder resulting from a number of factors in which an absolute or relative deficiency of insulin or its function occurs. It is projected that by the year 2025, India alone would have 57 million diabetic patients mainly of Type 2 DM constituting 90% of the diabetic population (King H et al, 1998, Ramachandra. A H. Surekharani et.al, 2002). The most common life threatening disorder of type2 diabetic subject is coronary heart disease (CHD) several mechanisms have been proposed for the explanation of the antiatherogenic properties of high density lipoproteins (HDL), Among them paraoxonase (PON1) has raised special interest.PON1 is a calcium dependent esterase that is exclusively bound to the apolipoproteinA1 containing HDL fraction in serum (Steffi Koppasch, Jenspietzsch, 2003). *In-vitro* studies showed that PON1 prevents accumulation of lipoperoxides in low density Lipoproteins (MacknessM.I 1998). Moreover HDL associated PON1 is able to destroy oxidized phospholipids in modified LDLs, therefore reversing the proinflammatory actions of LDL(WatsonA D et.al, 1995).Oxidised LDL has been shown to be a causal pathogenic factor in the development of atherosclerosis (SteinberaD et.al, 1997). Decreased levels of PON1 activity have been found in patients with DM in several studies (Abott C.A, Mackness, Ikerlay et.al, 1995) and they have been related ti diabetic microvascular and macrovascular complications. The aim of the present study was to determine correlation between serum PON1activity and HDL levels in type2 diabetes predisposing to atherosclerosis.

**MATERIALS AND METHODS**

The study was conducted over a period of six months .The study includes 104 subjects, admitted in medicine department in narayana hospital. Out of 104 subjects 42 were diabetic patients without complications, 20 were diabetic patients with complications like diabetic retinopathy, diabetic nephropathy. 42 were controls. Blood samples were collected after 12hrs fasting 5mi blood was taken in a plain tube and serum was separated after centrifugation and serum HDL cholesterol ,serum paraoxonase1,Fasting serum glucose were estimated both in cases and controls. Fasting serum glucose was estimated by Glucose oxidase peroxidase method (Carl A, Burtis, Edward, 1999). Serum paraoxonase was estimated by spectrophotometric method using p-Nitrophenylacetate as substrate (Sarkar P.D, Shivaprakash, 2006). Serum HDL was estimated by enzymatic CHOD by PAP method 1(Rifai N, Bachori et.al 2001).

**RESULTS**

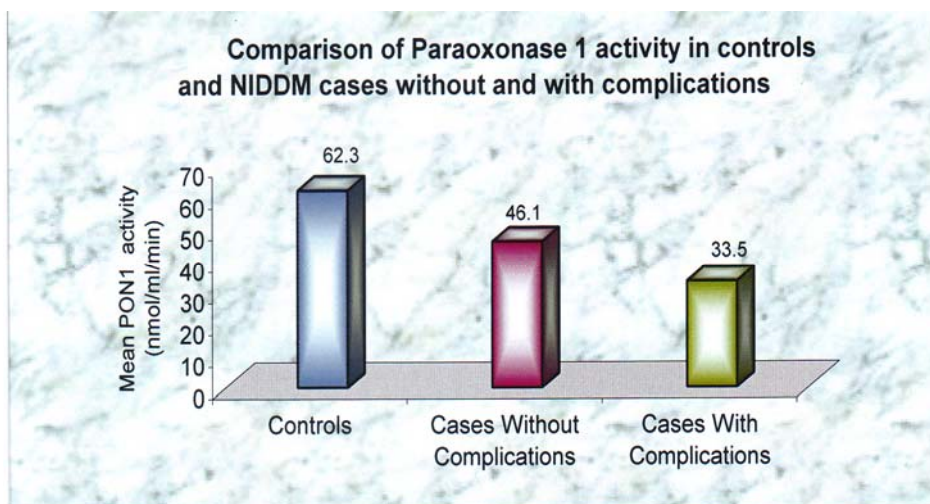
The results were expressed as mean (standard deviation). The p value was used to compare the patient mean value with control mean value. The mean and standard deviation of all parameters of the study were calculated in patients and control subjects. Within the study group relation between PON1 and HDL was assessed using pearsons correlation test with p value< 0.05 significant.

Table I shows the comparison of FSG, PON1, HDL in healthy controls and type 2 DM cases and Figure 1: shows comparison of Paraoxonase 1 activity in controls and NIDDM cases without and with complications, Figure 2: Shows Comparison of HDL-C levels in controls and NIDDM cases without and with complications in bar diagrams, Figure 3: shows the Relation between HDL & PON1 in scatter diagram.

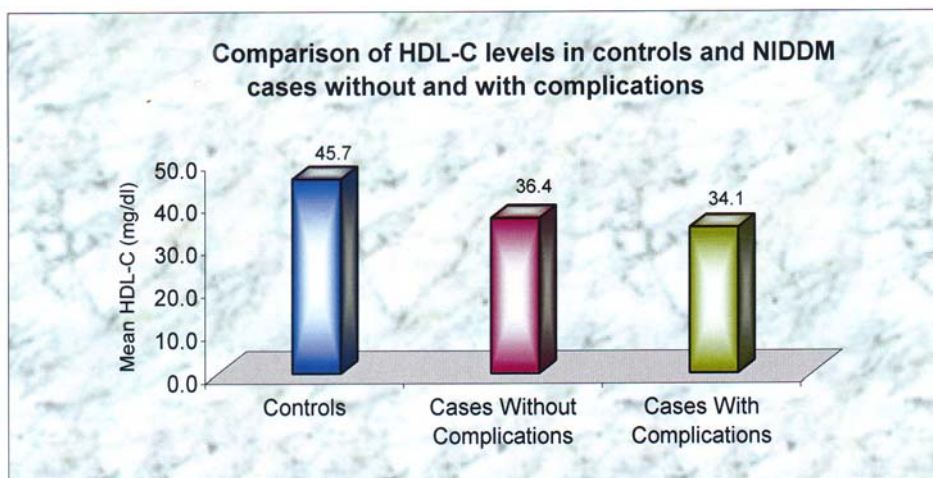
**Table : 1 comparison of FSG, PON1, HDL in healthy controls and type 2 DM cases**

		HDL (mg/dl)	PON1 (nmol/ml/min)	FSG (mg/dl)
Cases	62	35.7 ± 3.7	42.0 ± 8.1	95.2 ± 11.8
Controls	42	45.7 ± 7.8	62.3 ± 5.9	192.0 ± 61.7
Control vs Cases	T value	7.8	14.8	12.0
	P value	<0.001	<0.001	<0.001

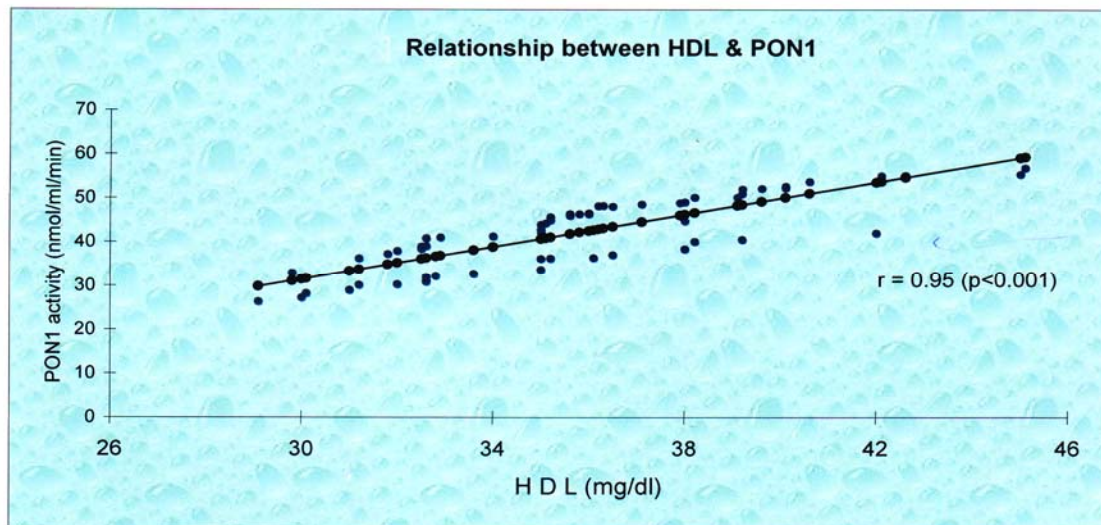
P <0.05 significant



**Figure 1: Shows comparison of Paraoxonase 1 activity in controls and NIDDM cases without and with complications**



**Figure 2: Shows Comparison of HDL-C levels in controls and NIDDM cases without and with complications**



**Figure 3: Shows the Relation between HDL & PON1**

## DISCUSSION

The present study observed that the mean values of PON1 activity in controls type 2 DM cases without complication and type 2 DM cases with complications were  $62.3 \pm 5.9$  nmol/ml/min,  $46.1 \pm 5.9$  nmol/ml/min and  $33.5 \pm 4.6$  nmol/ml/min respectively. It is evident that PON1 levels in type 2 DM subjects was low when compared to normal subjects and were statistically significant (Mackness M.I, Sarkar P.D) ( $p < 0.001$ ) and there was reduced HDL levels in type2 diabetic subjects. There was a positive correlation between PON1 and HDL levels ( $p$  value  $< 0.001$ ) in type2 diabetic patients several DM associated explanations of changes of PON1 activity are possible. First conformational changes of the enzyme as a result of glycooxidation and/or Lipoxidation processes (Baynell IW, 2000) could alter its activity. As indication, invitro glycation of purified paraoxonase protein can cause a 40% reduction in enzymatic activity (Hedrick G.G.). Second change in physiochemical properties of the HDL particle or in HDL metabolism could influence PON1 activity (Ferrettig Bacchetti T marchinnic caldarelli et.al 2001). Recently it is found that size reduction and accumulation of unesterified cholesterol in the HDL particle may impair the capacity of HDL to facilitate PON1 release from cells and to stabilize the enzyme. Hence in diseases like diabetes where HDL size is often reduced PON1 secretion is affected. Reduced levels of serum HDL is an independent risk factor for atherosclerosis.

Finally hormone and glucose homeostasis could affect PON1 activity. In conclusion our study support the view thatPON1 acts as an antioxidant in HDL and have a great impact in preventing LDL oxidation or destroying specific oxidized Lipoprotein constituents in the circulation. There by reducing risk of atherosclerosis. Hence PON1 activity along with HDL can be used for the diagnosis of onset of vascular complications in diabetes mellitus.

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