

## Original article:

# Paraoxonase 1, total cholesterol and HDL cholesterol in diabetes mellitus

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### Abstract

**Background:** Diabetes mellitus (DM) refers to a group of common metabolic disorder that shares the phenotype of hyperglycemia. The existence of hyperglycemia produces increased oxidative stress and associated with an increased risk of cardiovascular disease (CVD). The present study was planned to measure the serum levels of paraoxonase 1 (PON 1) activity, total and high density lipoprotein (HDL) cholesterol in patients with type 2 diabetes mellitus and to compare with healthy controls.

**Material and Methods:** In this study total 80 subjects were included above 40 years of age. 40 clinically diagnosed type 2 diabetic patients and 40 normal subjects were recruited as control. PON 1 activity , total cholesterol and HDL cholesterol levels were measured by the methods of Therry FD et al and Lopes Virella M et al respectively. Data were analyzed using 't' test for their level of significance.

**Results:** The mean PON 1 activity in type 2 diabetic patients was significantly lower than in the controls. The mean total cholesterol levels were significantly higher in patients as compared to the control subjects while the mean value of HDL cholesterol was significantly lower in type 2 diabetics when compared with controls.

**Conclusions:** Reduced serum PON 1 activity, HDL cholesterol and elevated total cholesterol level might contribute to the increased susceptibility for the development of CVD in type 2 diabetic patients.

**Key-words:** Type 2 diabetes mellitus, PON 1, HDL cholesterol

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### Introduction

The prevalence of type 2 diabetes mellitus is increasing and by the year 2025, the total number of people with diabetes is projected to reach 330 million worldwide. The region most likely to experience the main brunt of the epidemic is Asia. Here, diabetes could become two or three times more common than it is at present. Over the next 25 years, India alone is expected to see an increase from 36 to 73 million people with diabetes; majority of the cases being type 2 diabetes mellitus. [1, 2]

Traditionally, type 2 diabetes is thought of as a disease of the middle aged and elderly. [3] However, in recent decades, the world is facing a threat from

early onset type 2 diabetes frequently seen in children and adolescents. It is a hard fact that type 2 diabetes in the young is evolving as an epidemic and not a myth. This has great implication for health care burden in any country. [4-6]

Type 2 diabetes mellitus is part of the metabolic syndrome with a cluster of several abnormalities, including insulin resistance, dyslipidemia, cardiovascular disease (CVD) which in part might be due to abnormalities in lipid and lipoprotein metabolism. Dyslipidemia, frequently occurring in type 2 diabetes mellitus, might play a critical role in accelerated macro vascular atherosclerotic disease formation and may contribute significantly to the excess risk of CVD in type 2 diabetes patients. [7]

Therefore, the present study was designed to measure the biochemical parameters, considered as anti-risk factors and risk factors of CVD in type 2 diabetic .

#### **Material and Methods**

The present study was carried out in the Department of Biochemistry, Government Medical College, Miraj. The Study group included 40 patients diagnosed by clinicians as type 2 diabetes mellitus and above 40 years of age. Diagnosis was confirmed by performing fasting blood glucose and glycosylated hemoglobin determinations. Control group included 40 healthy controls without any family history of diabetes and no abnormal clinical findings and matching in age with study group. Patients with myocardial infarction, renal diseases, coronary heart disease and type 1 diabetes mellitus were excluded from this study. The Institutional Ethics Committee approved the study and consent was obtained from each participant in the study.

Fasting blood samples were collected taking all the aseptic precautions. PON 1 activity was assayed on fresh sample and sera were stored frozen at  $-20^{\circ}\text{C}$  for further analysis. PON 1 activity was determined by spectrophotometric assay of Therry FD et al in which phenyl acetate was used as a substrate.<sup>[8]</sup> Total cholesterol and HDL cholesterol were determined by Wybenga and Pileggi Method.<sup>[9]</sup>

**Statistical analysis:** All statistical analyses were performed using Minitab software. The data of patients and controls was analyzed by student's 't' test. P values  $< 0.001$  were considered significant.

#### **Results and Discussion**

In a study by Mackness et al, significantly lower PON 1 activity was seen in diabetic patients with familial hyperlipidemia.<sup>[10]</sup> But in other two studies, association between low PON 1 activity, impaired glucose metabolism and type 2 diabetes mellitus has not been observed.<sup>[11, 12]</sup> Because of contradictory reports regarding PON 1 activity, we

decided to assay the activity of PON 1 in type 2 diabetic patients. In the present study, the mean PON 1 activity was significantly decreased in diabetic patients as compared to that of controls (Table 1,  $P < 0.001$ ). Paraoxonase 1 is an antioxidant, HDL bound enzyme. It prevents low density lipoprotein (LDL) oxidation and therefore retards atherosclerosis. Oxidation of LDL is recognized as an early stage in the development of atherosclerosis, leading to LDL uptake by the macrophage scavenger receptor and hence to formation of foam cells. PON 1 can destroy active lipids in mildly oxidized LDL and protect against the induction of inflammatory responses in arterial wall cells.<sup>[13]</sup>

In our study, the mean serum total cholesterol level was significantly higher and HDL cholesterol was significantly lower in type 2 diabetic patients as compared to controls (Table 1,  $P < 0.001$ ). High level of serum cholesterol is an indicator for diseases such as CVD. HDL has a protective role against the development of atherosclerosis because of its role in reverse cholesterol transport.<sup>[14]</sup> Low concentration of HDL increases the risk for atherosclerotic diseases, which is one of the major diabetic complications leading to CVD.<sup>[15]</sup>

To conclude, reduction in the antioxidant enzyme PON 1 can lead to accumulation of superoxide radicals and failure of prevention of oxidation of LDL. This can lead to oxidative stress, endothelial cell damage and inflammation. These processes may further impair insulin action and might result in insulin resistance. Elevated level of total cholesterol and low level of HDL cholesterol increases the risk for atherosclerotic diseases. Hence periodic assay of PON 1 along with total and HDL cholesterol will help the physician in treatment and management of the diabetic patients and for decelerating the process of atherogenesis and development of CVD.

**Table No. 1 : Paraoxonase 1 Activity, Serum Total Cholesterol and HDL Cholesterol Levels in Diabetic Patients and Controls**

Subjects	PON 1 U/ml	Total Cholesterol mg/dl	HDL Cholesterol mg/dl
	Mean ± SD	Mean ± SD	Mean ± SD
<b>Patients</b>	81.05 ± 6.11*	241.1 ± 56.8*	19.96 ± 5.33*
<b>Controls</b>	103.32 ± 8.25	190.4 ± 19.9	42.27 ± 7.27

The statistical method used to compare data was 't' test. \*P<0.001 – highly significant.

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