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PARAOXANASE ACTIVITY AND ITS CONCENTRATION IN TYPE2 DIABETES MELLITUS

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ABSTRACT

Human serum paraoxonase is a high density lipoprotein (HDL) associated enzyme capable of hydrolyzing diverse substrates from organophosphate toxins to oxidized Phospholipids and possibly in the prevention of LDL lipid peroxidation. We investigated the serum activity and concentration of paraoxonase levels and fasting blood glucose levels in 104 subjects (42 patients with type2diabetes without Complications, 20 patients with type2 diabetes with complications, 42 controls were taken. Patients with type2 diabetes with complications had lower Paraoxonase activity than those without the complications. These results suggest that decreased PON activity in patients with type2 diabetes were involved with diabetic vascular complications

Keywords; Type2 diabetes mellitus (type2DM), Paraoxonase (PON1), Lipid peroxidation, Atherosclerosis. High density Lipoproteins (HDL) , Low density Lipoprotein (LDL)

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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 diabetics mainly of type2 DM constituting 90% of the diabetic population [1, 2, 3]. The most common and life threatening disorder that besets type2DM subjects is coronary heart disease (CHD).Irrespective of the ethnic background the risk of CHD among diabetic subjects is greater by a factor of 2 to 4 compared to non- diabetic subjects.[4] Recent experimental findings suggest that overproduction of reactive oxygen species may be involved in the initiation and development of vascular complications in diabetes[5,6]. Oxidation of low density lipoprotein particles and cytotoxic effects of lipid peroxides enhance the formation of foam cells and atherosclerosis, the intensity of lipid peroxidation and activity of the antioxidant defense system significantly change.[7] HDL levels are inversely related to the risk of developing atherosclerosis, human serum paraoxonase is a glycoprotein synthesized in the liver and secreted into the blood, where it associates with the HDL and has been implicated in the detoxification of organophosphate and possibly in the prevention of LDL lipid peroxidation.[8] by its paraoxidase activity and by preventing homocysteinylation of Apo B-100[9].Low serum paraoxonase activity has been associated with increased susceptibility to atherosclerosis which could be due to reduced capacity to detoxify lipid peroxides in diabetes. The aim of the study is to evaluate antioxidant role of paraoxonase in type2 DM in reducing the risk of lipid peroxidation.

MATERIALS AND METHODS

The study was conducted over a period of six months .The study includes 104 subjects recruited in medicine department in Narayana Hospital. Out of 104, 42 were patients of type2 DM without complications, 20 patients of type2 DM with complications (with diabetic retinopathy, diabetic nephropathy) and 42 were controls matched to the age and sex. Inclusion Criteria: Controls are healthy individual's age and sex matched without any major illness, Cases Type II Diabetes patients. Exclusion Criteria: Type II diabetes patients for alcoholics, smokers, Infectious disease. Were taken for the study blood samples were collected after 12hrs of fasting for estimation of fasting blood glucose and 2ml blood is collected in a plain tube for serum paroxonase estimation. This procedure is carried out both in cases and controls.FBS was estimated by Glucose oxidase peroxidase method.[10]

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Serum paraoxonase was estimated by spectrophotometric method[11] using P-nitro phenyl acetate as substrate.

RESULTS

The data analysis was done using SPSS software. The results were expressed as Mean (standard deviations) and range values. Student t test were group wise comparison. The p value of 0.05 was considered for statistical significance. The mean and standard deviation of all parameters of the study were calculated in patients and controls.Table I show the comparison of FBS, PON1 in healthy controls and type 2 DM Cases with and without complications. Figure I show the comparison of FBS in healthy controls and type 2 DM cases in bar diagram Figure II shows the comparison of PON1 in healthy controls and type 2 DM cases in bar diagram

Table: I

Comparison of FBS,. PON1 in healthy controls and type 2 DM Cases with and without complications.

Groups	No	FBS mg/dl	PON1 nmol/ml/min
Controls	42	95.2 ± 11.8	62.3 ± 5.9
Cases	62	192.0±61.7	42.0 ± 8.1
Control Vs Cases	t value	12.0	14.8
	p value	<0.001	<0.001

Figure I

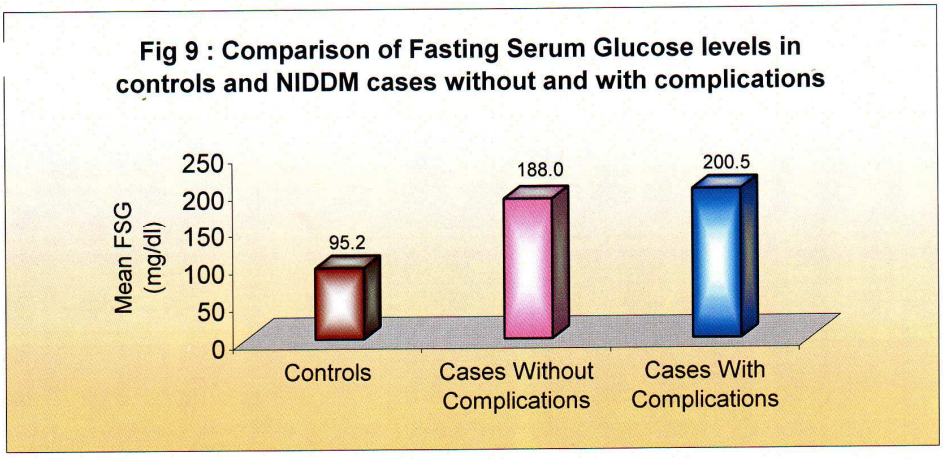
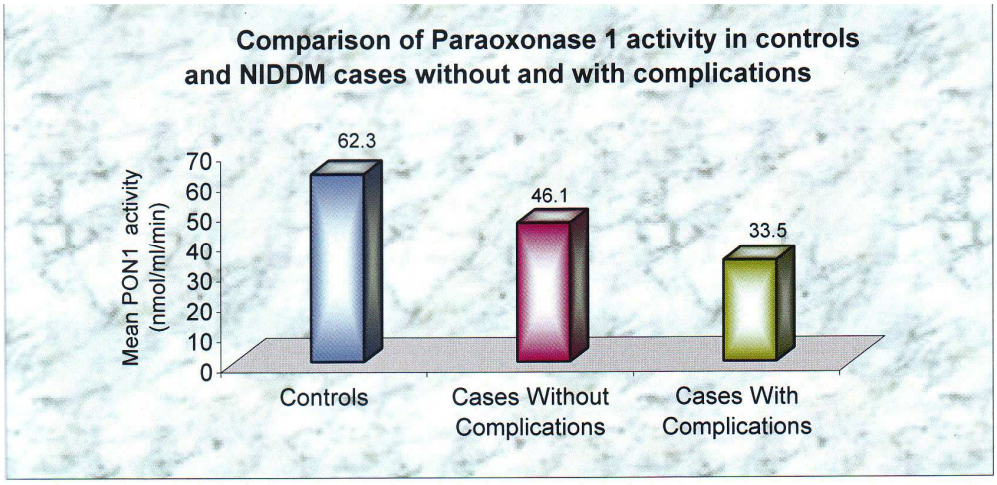


Figure II



DISCUSSION

Hyperglycemia, a hallmark of diabetic condition depletes natural antioxidants and facilitates the production of reactive oxygen species (ROS) which has the ability to react with all biological molecules like lipids, proteins, carbohydrates, DNA.etc and exert cytotoxic effects on cellular components.[12]
High levels of glucose are associated with non-enzymatic glycation of both extra and intracellular proteins. The accumulation of sorbital via the aldose reductase pathway, the activation of protein kinesics isoforms and reduced availability of nitric oxide (NO). The occurrence of free radical induced lipid peroxidation causes considerable changes in the cell membrane[13]. Peroxidation of lipid membrane has been related to the pathogenesis of many degenerative diseases, such as atherosclerosis, oxidative damage to DNA, ageing and DM.[14].

In our study the mean values of FBS in cases with complications, cases without complications, controls were 200.5±88.7 mg/dl,188.0±44.4mg/dl and 95.2±11.8mg/dl respectively. It was evident that the serum glucose levels were increased in type2DM cases with complications when compared to controls and were statistically significant (0.001). Similarly mean values of PON1 activity in cases with complications, cases without complications and controls were33.5±4.6nmols/ml/min,46.1±5.9nmols/ml/min and62.3±5.9nmols/ml/min.It was evident that PON1 activity was decreased in cases when compared to controls and were more decreased in cases with complications when compared to cases without complications and were statistically significant($p<0.001$). [8,11]

PON1 is an esterase associated with HDL it acts like an antioxidant, prevents lipid peroxidation of LDL[15].
Decreased levels of PON1 in type2 DM may be due to increased glycation of various plasma enzymes due to increased glucose concentration which further reduce the capacity of PON1 to prevent lipid peroxidation leading to increased tendency for lipid peroxidation and producing complications like diabetic retinopathy, neuropathy and atherosclerosis.
Hence present study supports the view that PON1 is a parameter which can be used to assess the early detection of complications in type2 DM.

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