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Serum levels of nitric oxide among diabetic patients and its correlation with lipid profile and oxidative stress

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Abstract
Background: Diabetes mellitus is a disease with a rapidly increasing prevalence. The present study was conducted to assess the serum levels of nitric oxide (NO) among diabetic patients and its correlation with lipid profile as well as oxidative stress.
Materials and Methods: 150 cases of type II diabetes were divided into three groups: Group I was type 2 diabetics with dyslipidemia and hyperuricaemia, group II was type 2 diabetics with dyslipidemia and normouricaemia and group III was type 2 diabetics with normolipidemia and normouricaemia. Patient was subjected to estimation of lipid profile. Nitric oxide level was determined.
Results: Group I had 35 males and 15 females, group II had 20 males and 30 females and group III had 25 males and 25 females. The mean nitric oxide level (µmol/L) in patients with increased triglyceride level in group I was 46.2, 72.0 in group II and 74.2 in group III and in patients with increased cholesterol level was 34.2 in group I, 54.6 in group II and 72.4 in group III, in patients with increased HDL level was 45.2 in group I, 58.4 in group II and 76.0 in group III and in patients with increased LDL level was 42.0 in group I, 60.4 in group II and 72.1 in group III. There was poor correlation of antioxidants with NO in all groups.
Conclusion: Oxidative stress parameters had poor correlation with NO level in all the groups.

Keywords: Antioxidant, nitric oxide, triglyceride

Introduction
Diabetes mellitus is a disease with a rapidly increasing prevalence needing continue research for new methods to both avert and treat this disorder. Now it is understandable that obesity and decreased physical activity are the well- known major risk factor for the progress of diabetes. Recently the prominence is focused on oxidative stress in pathogenesis of type two diabetes mellitus and its complication [1].

Endothelial dysfunction appears to be a reliable finding in all diabetic patients. Certainly, there is a general agreement that chronic hyperglycemia and DM lead to impairment in nitric oxide (NO) production and activity. NO is a short-lived gaseous free radical secreted by endothelium. Alterations in its bioavailability have been found to cause endothelial dysfunction, increasing susceptibility to hypertension, progression of atherosclerosis, hyper-cholesterolemia, thrombosis, stroke, DM and its chronic complications.NO is synthetized as a by-product of the conversion of its physiological precursor L-arginine to L-citrulline by a family of NO synthases (NOS). These enzymes comprise three distinct isoforms, encoded by three different genes: neuronal inducible (iNOS/NOS-2), and endothelial (eNOS/NOS-3) forms [2].

NO is synthesized as a by-product of translation of its physiological precursor L-arginine to L-citrulline. This reaction is catalysed by a family of enzymes known as NO synthases (NOS). Nitric oxide is produced in endothelial cells from the substrate L-arginine via eNOS [3]. Elevated asymmetric dimethyl arginine levels cause eNOS uncoupling, a mechanism which leads to decreased NO bioavailability. The endothelial dysfunction associated with diabetes has been attributed to lack of bioavailable NO due to reduced ability to synthesize NO from L-arginine [4] New basic research insights provide possible mechanisms underlying the impaired NO bioavailability in type 2 diabetes. So, the nitric oxide is reduced in the course of vascular disease [5] The present study was conducted to assess the serum levels of nitric oxide (NO) among diabetic patients and its correlation with lipid profile as well as oxidative stress.

Materials and Methods

The present study was conducted among 150 cases of type II diabetes of both genders. All were informed regarding the study and their consent was obtained.

Data such as name, age, gender etc. was recorded. Diabetes mellitus was diagnosed based on random blood glucose level >200 mg/dl or fasting plasma glucose >126 mg/dl or HbA1C>6.5% or impaired oral glucose tolerance test with two hours postprandial plasma glucose level > 200mg/ dl. The patients were divided into three groups: Group I was type 2 diabetics with dyslipidemia and hyperuricaemia, group II was type 2 diabetics with dyslipidemia and normouricaemia and group III was type 2 diabetics with normolipidemia and normouricaemia. Patient was subjected to estimation of lipid profile such as total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), very low-density lipoprotein (VLDL), high density lipoprotein (HDL), and serum creatinine levels. Nitric oxide was determined by a colorimetric kit that used a convenient measure of stable decomposition product total nitrate/nitrite. Results thus obtained was subjected to statistical analysis. P value less than 0.05 was considered significant.

Results

Table I: Distribution of patients

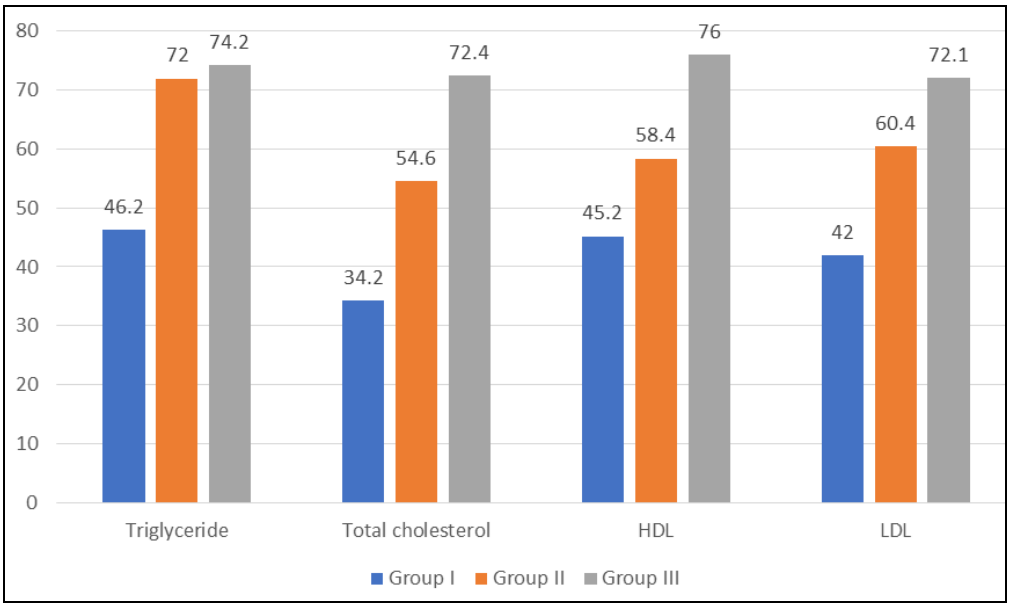
Groups	Group I	Group II	Group III
Male	35	20	25
Female	15	30	25

Table I shows that group I had 35 males and 15 females, group II had 20 males and 30 females and group III had 25 males and 25 females.

Table II: Assessment of nitric oxide (µmol/L) levels in patients

Lipid profile	Group I	Group II	Group III	P value
Triglyceride	46.2	72.0	74.2	0.04
Total cholesterol	34.2	54.6	72.4	0.02
HDL	45.2	58.4	76.0	0.01
LDL	42.0	60.4	72.1	0.05

Table II, graph I shows that mean nitric oxide level (µmol/L) in patients with increased triglyceride level in group I was 46.2, 72.0 in group II and 74.2 in group III and in patients with increased cholesterol level was 34.2 in group I, 54.6 in group II and 72.4 in group III, in patients with increased HDL level was 45.2 in group I, 58.4 in group II and 76.0 in group III and in patients with increased LDL level was 42.0 in group I, 60.4 in group II and 72.1 in group III. The difference was significant ($P < 0.05$).



Graph I: Assessment of lipid profile in patients

Table III: Correlation of nitric oxide with antioxidants

Correlation of NO with	Group I		Group II		Group III	
	r	p	r	p	r	p
MDA (nmol/l)	0.13	0.28	-0.12	0.32	0.05	0.71
SOD (Umg/ml)	0.08	0.45	0.16	0.19	0.23	0.02
CAT (Umg/ml)	-0.14	0.27	0.02	0.74	-0.05	0.72
GR (Umg/ml)	0.072	0.54	-0.016	0.73	-0.091	0.42
GPx (Umg/ml)	0.17	0.18	-0.041	0.71	-0.122	0.31

Table III shows poor correlation of antioxidants with NO in all groups.

Discussion

In diabetic patients, hyperglycemia excites the creation of advanced glycation end products (AGEs), and enhances the polyol, protein kinase C (PKC) and hexosamine pathways, which may lead to oxidative stress.[6] Then, excessive reactive oxygen species (ROS), such as superoxide anion (O2), react rapidly with NO radicals, forming the peroxynitrite anion, which is a toxic oxidant capable of damaging several biological molecules, leading to tissue injury. NO is oxidized *in vivo*, producing the stable NO products nitrate and nitrite (NOx) [7]. Numerous discoveries propose a causal relationship between NO and plasma levels

of NOx and, then, NOx plasma measurements reflect NO bioavailability. Nevertheless, over-production of peroxynitrite can deplete no bioavailability [8]. The present study was conducted to assess the serum levels of nitric oxide (NO) among diabetic patients and its correlation with lipid profile as well as oxidative stress.

In present study, group I had 35 males and 15 females, group II had 20 males and 30 females and group III had 25 males and 25 females. Ghosh *et al.* [9] compared serum nitric oxide level among type 2 diabetic patients along with other biochemical parameters and to compare it with that of normal population. 50 type 2 diabetics compared to 100 non-diabetics. There was significant difference when age- and sex-matched cases and controls were compared in regard to waist circumference and body mass index. The values of fasting and postprandial serum glucose, and lipid profile between study group and control group differed significantly. The mean serum level of NO in the study and control group was 43.83 ± 11.3 µmoles/L and 58.85 ± 12.8 µmoles/L respectively, and this difference was statistically significant.

We found that mean nitric oxide level (µmol/L) in patients with increased triglyceride level in group I was 46.2, 72.0 in group II and 74.2 in group III and in patients with increased cholesterol level was 34.2 in group I, 54.6 in group II and 72.4 in group III, in patients with increased HDL level was 45.2 in group I, 58.4 in group II and 76.0 in group III and in patients with increased LDL level was 42.0 in group I, 60.4 in group II and 72.1 in group III. Kumar *et al.* [10] assessed the serum levels of nitric oxide (NO) among diabetic patients and its correlation with lipid profile as well as oxidative stress in north Indian setting. The patients were divided into three groups: Group I- Type 2 diabetics with dyslipidemia and hyperuricaemia, Group II- Type 2 diabetics with dyslipidemia and normouricaemia and Group III- Type 2 diabetics with normolipidemia and normouricaemia. The nitric oxide level was significantly lower in Group I and Group II than Group III. The oxidative stress parameters had poor correlation with NO level in all the groups.

Various studies found that subjects with type 2 diabetes displayed decreased NO production which was related to confounding factors such as age, body mass index, and lipid profile. Researchers have reported that subjects with diabetes have an unfavourable lipid profile and altered plasma levels of oxidative stress markers like nitric oxide, and the NO levels were lower than in control subjects [11, 12].

The limitation of the study is small sample size.

Conclusion

Authors found that oxidative stress parameters had poor correlation with NO level in all the groups.

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