Serum Total Antioxidant Correlates With Hyperglycemia And Dyslipidemia In Diabetes Mellitus

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Abstract

Sustained accessibility to potent diabetic drugs by the majority of diabetic patients is uncommon in Nigeria. With epidemiological evidence that suggests oxidative stress as a risk factor in the pathogenesis of diabetes mellitus and diabetic complications, there is the need to determine the relationship of diabetes mellitus and its complication with total antioxidant**.** Outcome of such work will determine the need or otherwise for antioxidant supplement in the future management of diabetes mellitus. The study was carried out at the University of Maiduguri Teaching Hospital, Nigeria. Eighty eight diabetic patients and 30 age and sex matched controls were studied for total antioxidant status and lipid profile.

Comparison of mean plasma total antioxidant status between diabetic patients and non diabetic subjects was also done.

Mean serum total anti oxidant was significantly lower in diabetics than in control subjects (mean ± SD: 0.7 ± 0.35 vs. 1.6 ± 2.0mmol/L; $P<0.05$).There is an inverse relationship between serum total antioxidant and plasma glucose ($r = -0.9$; $P<0.05$). Significant relationship was found between total serum antioxidant and serum lipid in diabetics (cholesterol, $P<0.05$ and serum triglyceride, $P<0.05$)

Serum total antioxidant correlates with hyperglycemia and lipidemia in diabetics.

Keywords: Diabetes mellitus, lipidemia, antioxidant.

Introduction

Diabetes mellitus is a group of metabolic disorders of carbohydrate metabolism characterized by chronic hyperglycemia due Either to insulin deficiency, decreased insulin action or both.[1] Relative or absolute insulin lack is the cause of diabetes mellitus but details of hyperglycaemia induced complications are yet to be clearly elucidated. However, glucose auto oxidation commonly found in sustained hyperglycemic state is reported to reduce the capacity of antioxidant defense system.[2] Recent cell studies and animal models have demonstrated hyperglycemia reacting non-enzymatically with glycated biomolecules,[3] and proteins[4] that strongly contributes to the syndromic manifestation of diabetes mellitus and its complications.[5] Considering the huge resources required to deliver sustainable healthcare to diabetics and the predominant poverty in the sub-Saharan region, more efforts to elucidate the pathogenetic mechanism of diabetes mellitus and accessibility to affordable modalities of disease management is advocated. Therefore, the study aims at finding out the relationship of plasma total antioxidant and diabetes mellitus; and diabetic dyslipidemmia in a Nigerian population.

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Methods

The study was a case control study conducted at the University of Maiduguri Teaching Hospital, Nigeria from June 2006 to June, 2007. The Hospital is a tertiary referral centre for the six northeastern Nigerian states with some patients from bordering Cameroon, Chad and Niger Republics attending. Eighty eight diabetic patients diagnosed according to the World Health Organization criteria for the diagnosis of diabetes mellitus were consecutively recruited from the general outpatient clinic for the study. Control subjects were 30 healthy volunteers with blood glucose below diabetic cut off values.

Five milliliters (mL) venous blood sample was collected by aseptic procedure after 11-13 hours' fast from diabetic patients and control subjects. Two mL of the blood was aliquoted into fluoride oxalate bottle while the remaining emptied into new plain specimen bottle. The flouride bottle specimens were immediately centrifuged and plasma used for glucose assay while the serum was separated from the cells

immediately after clot retraction, and

Data obtained was analyzed using the statistical software SPSS Version 11.0 (spss, Chicago III, USA). Antioxidant kit from Randox laboratories Ltd., Ardimore, Diamond Road, Crumlin Co. Antrim, United Kingdom, BT 294 QY, Cat no NX 2332 was acquired for the study. Total antioxidant status was determined by Randox [R] reagent kit as described by the protocol of Miller et al,[6] where the free radical generated from the reaction of 2,2- Azino-di-3-ethylbenzthiazothine sulphate with metmyoglobin and hydrogen peroxidase reacts with antioxidant from the sample to produce a blue-green color. The concentration of the blue-green color is inversely proportional to the color produced.

Plasma glucose was determined by enzymatic method of Randox[R] where glucose reacts with glucose oxidase to produce hydrogen peroxide which reacts with peroxidase to produce an oxygen radical that reacts with the chromogen 4-Aminophenazone, to form a red-violet qinoneimine, whose concentration is directly proportional to the concentration of glucose in the sample.

Serum cholesterol was determined enzymatically using Biosystem[R] cholesterol kit as described by Meiattini et al.[7]

Serum triglyceride was assayed by glycerol phosphate, oxidase/peroxidase method of Biosystem[R] triglyceride kit as described by Fossati et al[8].While High Density Lipoprotein (HDL) cholesterol was determined after precipitation of serum by sodium tungstate using Biosystem[R] HDL kit as described by Grove.[9] Low density lipoprotein cholesterol was determined using Friedwald's formula.

(LDL cholesterol = Total cholesterol-Triglyceride/2.2 - HDL mmol/L.

Total Antioxidant assay was run in duplicates and antioxidant control Cat no. 2331was used in each antioxidant assay batch. Result of each batch was accepted only when control sera result is within acceptable control limits. Sample with values greater than 2.5mmol/L was diluted one in two with 0.9% normal saline and re-assayed. The means of the variables were compared using student's t-test and ANOVA. Correlation test between total antioxidant and lipid profile was also done.

Results

Male diabetics were more than female diabetics in the 20-39 years age group, while female diabetics were more than male diabetics in the age groups above 39 years. The reference values for serum total antioxidants for the control, insulin and non-insulin dependent diabetics is as presented in table I below, while the reference values for serum lipid profile is as presented in table II. Correlation between total antioxidant and short term glycemic control among diabetics and control subjects is shown in Table III. The correlation of serum total antioxidant and fasting blood glucose between control and both type I and type II diabetes mellitus were both significant ($r = -0.9$; $p<0.05$). Again the correlation of serum total antioxidant and two hour's postprandial glucose level between control and both type I and type II diabetes mellitus were significant ($p<0.05$). The correlation test between serum total antioxidant and lipid profile among the two classes of diabetes mellitus is shown in table IV.

Figure 1. Distribution of diabetics by age and sex.

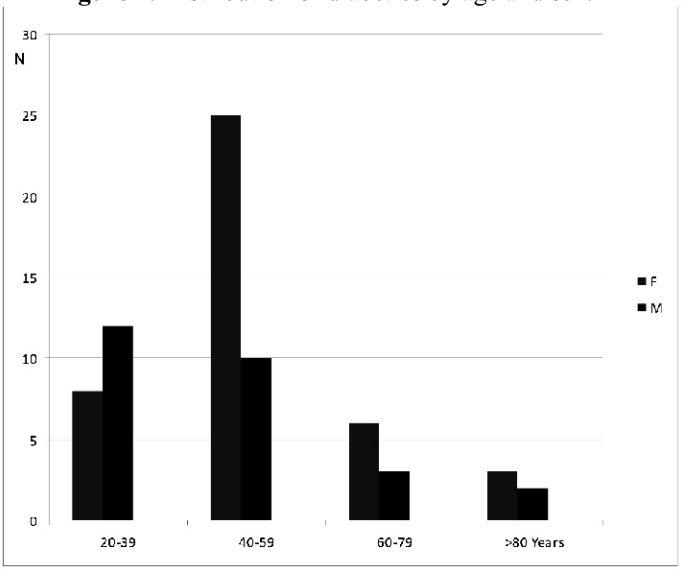

Table I. Comparison of mean values of serum total antioxidant in the studied groups.

Subjects	Mean ±SE (mmol/L)
Control	1.6 ± 2.0^a
Type I DM	0.7 ± 4.0^b
Type II DM	0.7 ± 0.3^b

Total antioxidant status is higher in control than in diabetics: $p<0.05$ for Type I DM and $p<0.05$ for Type II DM. No difference between Type I DM and Type II DM

Table II. Reference values of lipid profile for diabetics and control

GROUP	T.CHOLESTEROL Mean± 2SE Ref. limits	TRIGLYCERIDE Mean± 2SE Ref. limits	HDL Mean± 2SE Ref. limits	LDL Mean± 2SE Ref. limits
Control	4.2±0.12 2.7-4.2	1.3 ±0.03 1.0-1.6	1.3±0.07 0.7-2.0	2.3±0.12 1.0-3.4
Type I DM	5.8*±0.24 4.4-8.5	1.5±0.10 0.5-2.2	1.4±0.08 1.1-2.5	3.9*±0.21 2.6-6.1
Type II DM	6.0*±0.29 3.6-11.7	1.5±0.06 0.8-2.4	1.4±0.09 0.7-2.1	4.0*±0.19 0.7-9.0

*P<0.05 When control is compared with the respective group of diabetic patients

Table III. Correlation between total antioxidant status (TAS), f asting blood glucose and 2 hour's post prandial (2HPP)

	Type I DM	Type II DM
TAS vs FBG (r)	-0.853*	-0.702*
TAS vs 2HPP (r)	-0.858*	-0.723*

Inverse relationship between TAS and blood glucose * P<0.05

Table IV. Correlation between total antioxidant and lipid profile

	Type I DM	Type II DM
TAS vs TC	0.708*	0.347*
TAS vs TG	0.06*	0.306*
TAS vs HDL	0.543*	-0.378*
TAS vs LDL	-0.667*	-0.213*

* p<0.05

Discussion

The low serum total antioxidant observed in our diabetic patients is similar to the findings elsewhere. [10,11,12] Low antioxidant is explained in part by the hyperglycemia that generates superoxide, hydroxyl radicals and hydrogen peroxide free radicals through autoxidation and protein glycation.[13] Another explanation may be the facilitation of the polyol pathway of glucose metabolism that reduces antioxidant directly and indirectly by reducing antioxidant defense in patients with sustained hyperglycemia. The negative correlation of total antioxidant status and hyperglycemia found in the study is similar to the finding of Vadde [12] et al. This is explained by glucose autoxidation and polyol pathways that produce free radicals in diabetic patients.[12,14] Glucose, and often fructose spontaneously reduces molecular oxygen under physiological conditions to produce free radicals that accelerate the formation of advanced glycosylation end products,[15] which in turn generates more free radicals, a process referred to as glucose auto oxidation.[16,17] Free radicals are normally produced during aerobic cell metabolism,[18, 19] phagocytosis and immunological response to infection,[19, 20] and recent studies has shown evidence of pathogenic role in diseases.[20, 21] Failure of antioxidants to antagonize the toxicity of free radicals produces oxidative stress[22, 23] that leads to acute and chronic immune and non immune injuries to tissues.[18] The positive relationship between hyperglycemia and hyperlipidemia observed in this study is similar to the finding of Vadde [12] and can be explained by damage of lipids by free radicals resulting in derangement in lipid metabolism causing hyperlipidemia. Diabetes mellitus and its resultant complications like hypertension and nephropathy are increasing worldwide, with urban migration and increasing sedentary lifestyle in sub-Saharan Africa raising the incidence of diabetes mellitus and its complications. It is suggested that antioxidants is useful in the management of diabetes mellitus and its common complications like hypercholesterolemia, hypertension and cardiovascular diseases.[19,23]Our study confirms that there is negative correlation of total antioxidant status and hyperglycemia. We recommend building up the antioxidant level of diabetics with accessible, cheap dietary antioxidant sources available in the locality like carrot, palm oil, pumpkin, melon as suggested by other workers.[24,25] The traditional dietary control of diabetes mellitus of low carbohydrate should change to low carbohydrate and high antioxidant food stuff as supplementation of endogenous antioxidant enzymes is known to protect the organs from variety of injuries.[18] This is more so as diabetes mellitus healthcare is primarily a self-care requiring a good nutritional plan with short term and long term goals for optimal life style and

longevity by sustenance of desirable blood glucose concentration.[26,27]

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