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TOTAL ANTIOXIDANT STATUS IN TYPE 2 DIABETIC PATIENTS: EXPERIENCE AT UNIVERSITY COLLEGE HOSPITAL (UCH) IBADAN, NIGERIA

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ABSTRACT

Total antioxidant status (TAS) was measured in 20 Type 2 diabetic patients aged 40-60 years (mean 50 years). Patients were on diet and oral hypoglycemic drug therapy, with fasting plasma glucose (FPG) levels > 7.0mmol/L. Similar measurements were carried out in 20 apparently healthy individuals within the same age range (mean 46 years) and with FPG levels < 6.1mmol/L. FPG was measured by glucose oxidase method and TAS by a colourimetric method.

Comparing the two groups, TAS was significantly reduced in the Type 2 diabetic patients (0.96 ± 0.37 Vs 1.61 ± 0.16 mmol/L) ($P < 0.05$). An inverse correlation between FPG and TAS suggested the existence of a lower antioxidant defense in poorly controlled Type 2 diabetics. Good control of FPG, could possibly help reduce free radical activity and probably minimize the chronic complications in diabetic patients.

Key words: Type 2 Diabetes Mellitus, Reactive Oxygen Species [ROS], Antioxidants. *(Accepted 14 August 2006)*

INTRODUCTION

Evidence is on the increases that oxidative stress is a putative factor in the aetiology of many human disorder. By definition, oxidative stress arises when reactive oxygen species (ROS) generation exceeds the available antioxidant defenses. ROS, as the term implies, are chemically reactive molecules containing oxygen such as H_2O_2, HOCl and free radicals such as superoxide anion ($O_2^{\cdot}$), hydroxyl ($OH^{\cdot}$) radicals.[8, 9] Hence, in diseases in which the aetiology is linked with oxidative stress, ROS generation is either excessive or antioxidant defense levels are compromised such that they cannot deal with the normal ROS load.[8] When free radical production exceeds the available antioxidant defenses, the excess radicals react with all classes of biological molecules such as lipids, proteins, nucleic acid, etc, causing lipid peroxidation, protein denaturation, vascular injury and so on.[10,11] Generally, free radical activity is prevented by protective enzymes or scavengers known as antioxidants. These include enzymes like superoxide dismutase, catalase and glutathione peroxidase; endogenous proteins such as albumin, uric acid and chemical compounds such as vitamins C, E, and beta-carotene. [4,12,13] Some authors have reported that diabetic patients have significant defects of antioxidant protection which may increase their vulnerability to oxidative damage and the development of diabetes' complications.[14]

A recent study to assess the antioxidant levels in the blood of Type 2 diabetic patients in comparison with apparently healthy individuals, showed a significant decrease in total antioxidant status (TAS), albumin, ascorbate, urate and alpha-tocopherol in the diabetic patients.[14-16] The use of TAS, also known as the total radical trapping antioxidant parameter(TRAP), has been recently proposed as a way of assessing the antioxidant property of plasma.[15] The TAS takes into consideration both known and unknown antioxidants present in the plasma, as well as their mutual cooperation. It thus represents a more reliable estimation of plasma antioxidant capacity. It is therefore better than the separate measurements of each known antioxidant.[16] Measurement of TAS in Type 2 diabetic patients is thus a useful indicator of risk from disease associated with free radical activity. If TAS is low, this may indicate the need for antioxidant therapy[14]. This present study is intended to assess the TAS in a group of Nigerians with poorly controlled Type 2 diabetes mellitus.

SUBJECTS, MATERIALS AND METHODS

Twenty (20) Type 2 diabetic patients comprising 15 males and 5 females on diet restriction and oral hypoglycaemic drug therapy aged 40-60 years with FPG levels > 7.0mmol/L were recruited from the Metabolic Research Ward of University College Hospital (UCH) Ibadan, and used as test group after

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obtaining their Consent. Twenty (20) apparently healthy individuals comprising of 12 males and 8 females within the same age range who were not on any medication and are non-hypertensive were recruited as control after obtaining their consent as well. The control group consists of University College Hospital (UCH) workers and postgraduate students of the same institution. In selecting the control group, those with fasting plasma glucose level > 6.1 mmol/L were excluded from the study. 5ml of whole blood was collected from each subject after 12 hours overnight fast by clean venepuncture into fluoride
oxalate and heparinized bottles for FPG and TAS analyses respectively. The FPG level was estimated by a glucose oxidase method[17] and TAS by a colorimetric method.[18]

RESULTS

The mean [SD] body mass index (BMI) of Type 2 diabetics was 27.24 [6.77] Kg/m^2 while in healthy individuals it was 21.76 [2.41] Kg/m^2 (Table 1). There was a significant difference between the mean BMI of controls and diabetics ($p<0.05$). FPG and TAS levels were 9.65 [5.63]mmol/L and 0.96 [0.37] mmol/L respectively, for the diabetic patients, and 5.16 [0.58] mmol/L and 1.61 [0.16]mmol/L respectively, for the controls (Table 1). TAS was significantly reduced in the Type 2 diabetic patients ($p<0.05$) as compared to controls. An inverse correlation between the BMI/ TAS and also between FPG/TAS was found (Table 2).

Table 1: **Comparison of BMI, FPG and TAS levels in healthy N0n-diabetics and Type 2 diabetic patients.**

(n =20)

Group/ Variables	**Mean BMI**	**Mean FPG**	**MeanTAS**
	(Kg/m^2)± 2SD	**(mmol/L)± 2SD**	**(mmol/L) ± 2SD**
Diabetic	27.24± 6.77	9.65 ±5.63	0.96± 0.37
Non-diabetic	21.76±2.41	5.16±0.58	1.61±0.16

Table 2 : **Statistical correlations of TAS, BMI and FPG**

	FPG	TAS
	R(p-value)	r(p-value)
BMI	0.100(0.541)	-0.338(0.033)*
FPG	1.000	-0.513(0.001)**

** Correlation is significant at the 0.001 level (2-tailed)

*Correlation is significant at the 0.05 level (2-tailed)

DISCUSSION

Reactive oxygen species (ROS) have been implicated in the development[19] and the late complications[20] of diabetes mellitus. The diabetic patient is at significantly increased risk of developing vascular disease. Its aetiology may involve oxidative damage by free radicals and protection against such damage can be offered by radical scavenging antioxidants[14]

The use of TAS, also known as the total radical trapping antioxidant parameter (TRAP), has been recently proposed as a way of assessing the antioxidant property of plasma.[15] The TAS takes into consideration both known and unknown antioxidants present in the plasma, as well as their mutual cooperation. It thus represents a more reliable estimation of plasma antioxidant capacity. It is therefore better than the separate measurements of each known antioxidant.[16] Measurement of TAS in Type 2 diabetic patients is thus a useful indicator of risk from disease associated with free radical activity. If TAS is low, this may indicate the need for antioxidant therapy.[14]

In this study a significant reduction in TAS was observed in Type 2 diabetic patients. This finding suggests the existence of low level of circulating antioxidants in these patients. The decreased levels of TAS may be due to:

- More utilization of these antioxidants to remove excess free radicals produced as a result of diabetes mellitus.[21,22] The most likely sources of increased free radicals in diabetes mellitus are auto-oxidation of glucose[21] and non-enzymatic glycation.[22,23]
- Lower dietary intake of antioxidants such as vitamins C and E, beta-carotene and sulphur containing amino-acids such as methionine in the diet [4] as a result of poor socio-economic status of the individuals.
- Insufficient antioxidant enzyme synthesis such as superoxide dismutase (SOD) and glutathione peroxidase (GPx) which may in turn be due to decreased micronutrient availability such as selenium, zinc, copper and manganese.[4]

In this study, an inverse relationship between the BMI/TAS and FPG/TAS has been demonstrated. In addition, a positive relationship is observed to exist between BMI/FPG. This shows that as the BMI increases, there also exists a corresponding increase in FPG, which invariably leads to a significant decrease in TAS.

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