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## RESEARCH ARTICLE

### STATUS OF VITAMIN C, VITAMIN E AND GLUTATHIONE IN DIABETIC PATIENTS WITH AND WITHOUT DYSLIPIDEMIA

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#### ABSTRACT

Hyperglycemia in DM is associated with increased lipid peroxidation and excessive production of free radicals which lead to oxidative stress by autoxidation of glucose. It is an important pathogenic mechanism in the development of diabetes and its complications. The research work included 50 healthy controls and 100 patients with type 2 diabetes mellitus. Fasting blood samples collected using aseptic technique were evaluated for serum levels of the fasting blood glucose, triglycerides, total cholesterol, HDL, LDL, vitamin C, vitamin E and glutathione by spectrophotometric method. On the basis of lipid profile the patients were categorized into 2 groups diabetic with dyslipidemia and diabetic without dyslipidemia. It was observed that vitamin C, vitamin E and glutathione levels in serum are significantly depleted in diabetics with dyslipidemia as compared to diabetics without dyslipidemia and control.

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## INTRODUCTION

Diabetes is the commonest metabolic disorder affecting the people all over the world. Globally, the number of diabetes patients has risen sharply. Diabetes mellitus is a heterogeneous group of metabolic diseases that is characterized by chronic hyperglycemia and instability in carbohydrate, lipid, and protein metabolism resulting from defects in insulin secretion and/or insulin action (Abdel-Rahman, 2011) which leads to many disorders, mainly cardiovascular disease and early death. Most patients with diabetes have lipid metabolism disorders; most common forms are decreased high density lipoprotein (HDL-C) and increased triglyceride, cholesterol and LDL-c. Hyperglycemia was found to promote lipid peroxidation of low density lipoprotein (LDL) by a superoxide dependent pathway resulting in the generation of free radicals (Giacco and Brownlee, 2010). Generation of free radicals often worsen the complications of DM such as hypertension, atherosclerosis and microcirculatory disorders. There is emerging evidence that

diabetes leads to depletion of the cellular antioxidant defence system and increased levels of reactive oxygen species (Dincer et al., 2002). Moreover, Vitamin C and E are important antioxidant in humans, able of scavenging oxygen-derived free radicals, improved hyperlipidemia and decreased blood pressure (Caballero, 2004). Vitamin C is structurally similar to glucose and can replace it in many chemical reactions, and thus is effective in prevention of non-enzymatic glycosylation of proteins. Vitamin E is a lipid soluble antioxidant and protects LDL-c particles from oxidative attack (Afkhami-Ardekani et al., 2009). Antioxidants may help reduce the risk of heart disease and other complications in people with diabetes (Devaraj and Jialal, 2006). Glutathione is present in all living organisms and is very important for oxidation-reduction reactions in connection with the capacity of the sulfhydryl group (SH—) of cysteine to undergo the reversible reaction (Irshad and Chaudhuri, 2002). It is the major endogenous antioxidant produced by the cells, participating directly in the neutralization of free radicals and reactive oxygen compounds, as well as maintaining exogenous antioxidants such as vitamins C and E in their reduced (active) forms. Several studies showed increased oxidative stress, and decreased basal vitamin C and E levels in diabetic patients (American Diabetes Association,

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2009). Type 2 diabetes mellitus, hypertension and dyslipidemia are associated with insulin resistance and an increased risk of coronary heart disease. Therefore, reducing fat intake, increasing antioxidants, particularly vitamins C and E intake, should be encouraged (Kaviarasan et al., 2005). This study was planned to determine and compare the levels of vitamin C, vitamin E & Glutathione in T2DM patients with and without dyslipidemia to healthy controls.

## MATERIALS AND METHODS

The study was carried out in 50 healthy control and 100 clinical established and laboratory confirmed type 2 diabetic patients (fasting blood glucose > 126 mg/dl) who attended the outpatient department of Medicine of MBS Hospital, Kota during the year 2012-13. The institutional ethical committee approved the study protocol. The age of the patients ranged from 30 to 60 years.

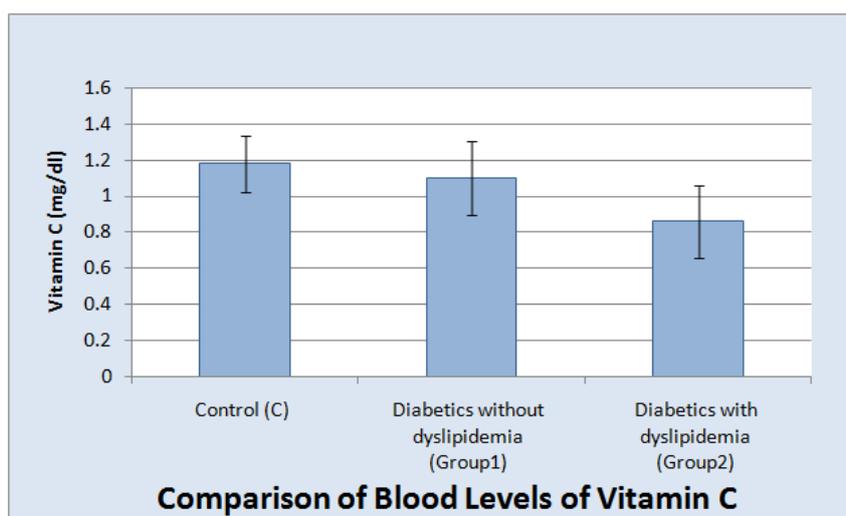
Fasting blood samples collected using aseptic technique were evaluated for serum levels of the fasting blood glucose, triglycerides, total cholesterol, HDL, LDL, Vitamin C and Vitamin E by spectrophotometric method. On the basis of lipid profile the patients were categorized into 2 groups diabetic with dyslipidemia and diabetic without dyslipidemia. Dyslipidemia was labelled based according to ATP (Adult Treatment Panel) III classification for lipid profile (Devaraj and Jialal, 2006). Data were analyzed using Microsoft Excel 2007 and results were expressed as Mean±SD.

## RESULTS

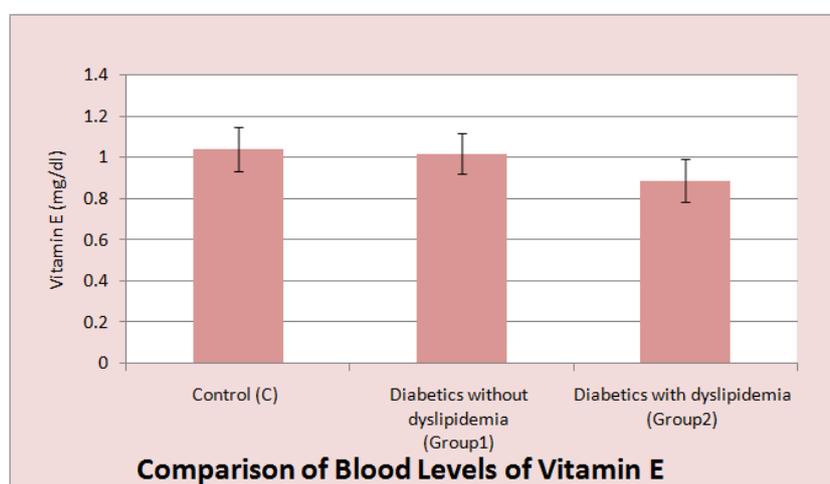
Total 100 type 2 diabetes mellitus patients included in study was segregated in 2 groups, group-1(Diabetics without dyslipidemia) and group-2 (Diabetics with dyslipidemia).

**Table 1. Comparison of Blood Levels of Vitamin C, Vitamin E and Glutathione in all the 3 Groups**

Parameters	Control (C) (Mean ± SD)	Diabetics without dyslipidemia (Group1) (Mean ± SD)	Diabetics with dyslipidemia (Group2) (Mean ± SD)	ANOVA	
				F score	P value
Vitamin C (mg/dl)	1.18 ± 0.154	1.10 ± 0.206	0.86 ± 0.201	49.77	3.11E-17,(p<0.05) Significant
Vitamin E (mg/dl)	1.04 ± 0.108	1.02 ± 0.097	0.89 ± 0.105	41.71	4.48E-15,(p<0.05) Significant
Glutathion (mg/dl)	31.1 ± 1.59	30.7 ± 1.61	28.9 ± 1.51	16.17	4.47E-07,(p<0.05) Significant



**Fig.1. Comparison of blood levels of vitamin C between different groups**



**Fig.2. Comparison of blood levels of vitamin E between different groups**

Group-1 include 41 diabetes patients (24 male and 17 female) with mean age of  $46.7 \pm 7.2$ , group 2 include 59 diabetes patients (27 male and 32 female) with mean age of  $46.9 \pm 7.6$  and control include 50 healthy subject (28 male and 22 female) with mean age of  $45.5 \pm 8.6$  years. Table shows that Vitamin C, vitamin E and Glutathion levels in serum are significantly depleted in Diabetics with dyslipidemia as compared to Diabetics without dyslipidemia and Control. Vitamin C and vitamin E are important nutrient antioxidants and deficiency of which may contribute to oxidative stress. (Table 1)

## DISCUSSION

Hyperglycemic conditions are associated with elevated ROS production, predominantly through mitochondrial electron transport chain and NADPH oxidase (Izuta *et al.*, 2010; Dymkowska *et al.*, 2014). Increased Oxidative stress has been widely established as a major contributory factor in the development as well as progression of diabetes and its complications (Giacco and Brownlee, 2010; Williams *et al.*, 2013). It has been suggested that insulin resistance may be accompanied by intracellular production of free radicals. Insulin has been found to increase the production of hydrogen peroxide in adipocytes cultured in vitro and this  $H_2O_2$  has been shown to mimic the action of insulin. Thus, a vicious cycle between hyperinsulinemia and free radicals could be operating in the early stages of diabetes pathogenesis. Insulin resistance induced elevated plasma free radicals, in turn, may cause a deterioration of insulin action, with hyperglycemia being a contributory factor (Ceriello, 2000). Hyperglycemia was found to promote lipid peroxidation of low density lipoprotein (LDL) by a superoxide-dependent pathway resulting in the generation of free radicals (Giacco and Brownlee, 2010). The present study demonstrated serum levels of Vitamin C, vitamin E and Glutathione are significantly depleted in Diabetics with dyslipidemia as compared to Diabetics without dyslipidemia and Control. (Fig.1, 2) Vitamin C and vitamin E are important nutrient antioxidants and deficiency of which may contribute to oxidative stress. It is also observed a significant decrease in high density lipoprotein cholesterol (HDL-C), reduced Glutathione (GSH), Glutathione peroxidase (GPx), Glutathione reductase (GR) and Superoxide dismutase (SOD) as compared to the control subjects. However the fasting blood sugar (FBS), post prandial blood sugar (PPBS), total cholesterol (TC), Triglyceride (Tg), low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) levels were found significantly increased as compared to the control subjects (Manjulata Kumawa *et al.*, 2012; Rajan and Naresh kumar, 2013). Accordance with Budin *et al.* (2009), who studied that both lipid accumulations and reduction in antioxidant activity contributed to the development of oxidative stress in diabetes (Budin Balkis *et al.*, 2009). Accordance with Mahmoud H and Mosaad, who was found that GSH is decreased statistically significantly in sera of patients with DM (Mahmoud H. Hadwan *et al.*, 2007; Mosaad A. Abou-Seif Abd-Allah Youssef, 2004). Our results are in agreement with Rahimia whose study indicated that the use of antioxidants reduces oxidative stress in diabetes (Rahimia *et al.*, 2005). It is also reported beneficial effects of oral vitamin C (1000 mg/day for 4 months) on glucose, lipid metabolism, and free radicals in T2DM (Paolisso *et al.*, 2007; Badr *et al.*, 2011).

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