

*Research Article***Vitamin C in endothelial dysfunction in patients with type 2 diabetes mellitus**

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**Abstract**

**Background:** To investigate the relationship between ascorbic acid level in serum and anti-oxidant parameters in blood with type 2 diabetes mellitus patients. **Patients and methods:** The study was conducted on 85 subjects, 25 as a control and 60 with type 2 diabetes. **Results:** The current study was done in the period between January 2016-December 2018. The study included 60 patients with type 2 DM. The duration of diabetes ranged from one month to 240 month with mean  $74.2 \pm 64.8$ . **Conclusion:** T2-DM patients with more severe diabetic nephropathy had lower vitamin C levels **Keywords:** Type 2 diabetes mellitus; Vitamin C; endothelial dysfunction

**Introduction**

In severe Oxidative stress (OS) cell damage may occur due to the low expression of antioxidant enzymes, is particularly sensitive to reactive oxygen and nitrogen species (RONS)<sup>(1)</sup>. These molecules may act on different substrates in the insulin intracellular signaling cascade, causing cell damage<sup>(2)</sup>.

This process is probably the common event for DM-2 complications with the hyperglycemia being the probable biochemical key involved in the induction of such pathways<sup>(3)</sup>. For Monnier & Colette<sup>(4)</sup>, both the activation of the OS and the excessive glycation of proteins caused by hyperglycemia appear as important components in the emergence of diabetic complications.

**Aim of the study**

To investigate the relationship between ascorbic acid level in serum and anti-oxidant parameters in blood with clinical, and duplex findings of brachial artery of patients with type 2 diabetes mellitus.

This prospective Cross sectional case control study was conducted in the period between (from January 2016-December 2018) at MINIA university hospital from the out-patient clinic.

The included subjects of the current study were 85 subjects: 63 females and 22 males and their ages ranged from 41-72 years old.

**Group 1:**

The control group (25 volunteers) will be selected as healthy participants of matched age and gender having no past history of any chronic medical illnesses.

**Group 2:**

Sixty (60) diabetic type 2 patients will be included among those attained to the MINIA university hospital out-clinic.

- Patients with other chronic medical illnesses
- Those with secondary diabetes or other endocrinal pathologies.
- Mental health problems (senile dementia and Alzheimer's disease, among others) will be excluded, as they configure vulnerable groups, beyond the scope of this study.

Laboratory studies; Duplex study; Echocardiography.

**Statistical studies:**

The collected data were coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 25.

The level of significance was taken at (P value < 0.05).

## Results

**Table 1: Echocardiographic parameters comparative analysis:**

		Control	DM	P value
		N=25	N=60	
<b>Ejection fraction of left ventricle</b>	<i>Range</i> <i>Mean ± SD</i>	(59-78) 65.4±4.9	(59-76) 65±4.2	0.678
<b>left ventricular diameter in diastole</b>	<i>Range</i> <i>Mean ± SD</i>	(3.1-5.1) 4.3±0.6	(3.2-6.3) 4.6±0.6	<b>0.034*</b>
<b>left ventricular diameter in systole</b>	<i>Range</i> <i>Mean ± SD</i>	(2.1-3.5) 2.8±0.4	(2.1-3.7) 2.9±0.4	0.060
<b>Left ventricle hypertrophy</b>	<i>Yes</i> <i>No</i>	0(0%) 25(100%)	9(15%) 51(85%)	0.053

In this table:

- 1- **The Ejection fraction of left ventricle was** ranged from (59-78), the mean was 65.4±4.9 in control, while in Diabetic group the range was (59-76) and the mean was 65±4.2.
- 2- **Left ventricular diameter in diastole** ranged from (3.1-5.1cm), the mean was 4.3±0.6 in control, while in Diabetic group the range was (3.2-6.3cm) and the mean was 4.6±0.6.
- 3- **Left ventricular diameter in systole was** ranged from (2.1-3.5cm), the mean was 2.8±0.4, while in Diabetic group the range was (2.1-3.7cm) and the mean was 2.9±0.4.
- 4- **Left ventricle hypertrophy was found 15% in diabetic, while not in 85% of diabetic group.**
- 5- As shown in this table regarding **Echocardiographic parameters**. There were statically significant difference between control and diabetic group regarding to **left ventricular diameter in diastole**.

## Discussion

Persistent hyperglycaemia in diabetes mellitus increases the production of reactive oxygen species (ROS) and activates mediators of inflammation as well as suppresses antioxidant defense mechanisms, ultimately contributing to oxidative stress which leads to endothelial dysfunction (ED) in diabetes. Furthermore, there is increasing evidence that ROS, inflammation and fibrosis promote each other and are part of a vicious connection leading to

development and progression of CVD and kidney disease in diabetes<sup>(5)</sup>.

In the current study; 35% of diabetic patients showed manifestations of peripheral ischemia and 30% of them showed diabetic retinopathy (P <0.001). They showed raised Systolic B.P. and diastolic B.P. highly significantly level (P=0.009& P<0.04 respectively) than control.

Endothelial dysfunction is one of the initial key steps in atherosclerosis in diabetic subjects. Several risk factors, such as hypertension, dyslipidaemia, inflammation, oxidative stress, and AGEs, are associated with atherosclerosis and micro- and macro-vasculopathies<sup>(6)</sup>. The mechanism of endothelial dysfunction (ED) in type 2-DM may be due to increased inactivation of endothelium-derived nitric oxide by oxygen-derived free radicals<sup>(5)</sup>.

Relationships between oxidative stress markers and antioxidants, point to vitamin C as a potential prognostic indicator of diabetic microangiopathy. All patients with long-standing diabetes used oral hypoglycemic drugs or insulin or both, and most of them were taking antihypertensive and cholesterol-lowering drugs, they showed the highest imbalance between the antioxidant status and increased concentrations of oxidative damage markers<sup>(5,7)</sup>.

In the current study; plasma levels of ascorbate, SOD, catalase and glutathione were highly significantly decreased, while plasma lipid peroxidation levels were highly significantly raised in patients' group than those of control (P= 0.001).

Urinary ACR, plasma total cholesterol and LDL were highly significantly raised in patients' group than that of control group (P= 0.001). The Plasma TG was insignificantly raised in diabetic patients' group (P=0.67).

These results agreed with those of <sup>(8)</sup> who showed that T2-DM patients with the highest Urinary ACR (greater than 300 mg/g) had the lowest levels of vitamin C and the highest urine albumin concentration. They found also that vitamin C levels correlated negatively with serum creatinine, urine albumin and UACR. Over all they concluded that T2-DM patients with more severe diabetic nephropathy had lower vitamin C levels.

Concentration of vitamin C was significantly lower in patients with metabolic syndrome (MS) than in the control group. Gender and age did not affect either the mean concentrations of vitamin C.<sup>(6)</sup>

In Type-2 DM, reduced serum antioxidant activity correlates with worsened glycemic control. Increased oxidative stress and low vitamin C levels were correlated with severity of diabetic neuropathy. SOD and vitamin C prevent the rapid inactivation of NO by superoxide anion<sup>(7)</sup>.

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