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The correlation between primary product and end product of lipid peroxidation in serum of patients with Diabetes Mellitus type II

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Abstract:-

This research includes comparison between some important biochemical in the diabetic patients type II .Blood samples were collected from (30) type II diabetic patients (15 male and 15 female),(30) control group (15male and 15 female) aged 36-46 years from different department of Al-Diwaniyah general hospital. There were significant differences p <0.01 in level malondialdehyde MDA between diabetic patients type II and control group were [(1.88±0.16µmol/l male,1.92±0.23 µmol/l female)] than control group [(0.91±0.32 µmol/l male,1.1±0.26 µmol/l female)]and significant differences p<o.o1 in level conjugated diene hydroperoxide between diabetic patients type II and control group were [(16.1 ±2.24 ±,15.6 ±2.37µmol/l female)]than control group [(9.4±2.3 µmol/l male,9.51±2.4 µmol/l female)].

Introduction:-

Diabetes mellitus is a very complex chronic disease with syndrome of hyperglycemia. It results from absolute or relative decease insulin secretion from ß-cell of the islets of langerhans. In1979, the National Diabetes Data Group (NDDG) developed a

Key word:- malondialdehyde MDA, conjugated diene hydroperoxide, Diabetes Mellitus type II.

classification and diagnosis scheme for diabetes mellitus. This design included dividing diabetes into two broad categories: type I, insulin dependent diabetes mellitus (IDDM) and type II, non-insulin-dependent diabetes mellitus (NIDDM) (1) type II diabetes is characterized by hyperglycemia due to an individual's resistance to insulin with an insulin secretary defect. This resistance results in a relative, not an absolute, insulin deficiency. Type II constitutes the majority of the diabetes cases. Most patients in this type are obese have an increased percentage of body fat distribution in the abdominal region. This type of diabetes is associated with a strong genetic predisposition with patients at an increased risk with an increase in age, obesity and lack of physical exercise and often goes undiagnosed for many years

(2,3). Lipid peroxidation is formed by oxidation of membrane poly unsaturated fatty acid that contain double or triple bonds (inter action of per oxidation aldehyde with phosphor lipids) leads to release of short- chain aldehdes such as malondialdehdyde (MDA)(4). Lipid peroxidation (LPO) is the most extensively studied manifestation of oxygen activation in biology. The end products of lipid peroxdation very commonly detected by the measurement of thiobarbituric acid reactive substance(TBARS) this assay has ,however, been criticized for the lack of specificity .Lipid peroxidation as measured by lipid hydroperoxides (5) have been shown to correlate closely with TBARS data in tissue and sample. With proper caution TBARS measurement may provide meaningful information (6). A low density lipoprotein (LDL) Particles has 2200 molecules of free fatty acid, half of which is PUFA which is a highly susceptible substrate for free radical reaction. Patient with DM have an increased risk of premature atherosclerosis, which may be due in part to increased oxidizability of LDL (7). LDL initially accumulates in the extra cellular space of subendothelial space of arteries and through the action of resident vascularcell ismildiy oxidized to form minimally oxidized LDL (OLDL). OLDL is internalized by the macrophages through scavenger receptor pathway.Native LDLis internalized by the classical receptor pathway with negative feed back so that internalized cholesterol down regulateLDLreceptor and prevent further internalization. Such negative feed back does not exist for scavenger path way. Hence,cholesterol accumulates in the arterial wall(8). In addition, OLDL inhibits release of Endothelial Derived Relaxation Factor (EDRF)and reduces the action of EDRF on the vessel wall OLDL stimulates endothelial cell to release a number of biologically active factors like growth factor for vascular cell chemotactic factors (so that resident monocytes are attracted). OLDL causes disturbance of eicosaniod homeostasis and platelets aggregation activates thymphocytes in the atherosclerotic lesion stimulating proliferation of smooth muscle cell. Taken all these together OLDL is atherogenic (9).

The aim of study:-

This study is amid to determination the correlation between primary product and end product of lipid peroxidation in serum patients with diabetes mellitus type II.

Experimental

Patients

We studied 30 type II diabetes patients (15male, and15 female aged 36-46years). All patients were diagnosed at the diabetes unit of AL-Diwaniyah general hospital. The study also included 30 healthy individuals, aged 36-46 years who not taken any medication.

Blood sample collection

Blood samples were drawn in the fasting state and processed within 20 min of collection .After clotting serum was separated by centrifugation and divided in three aliquots.

Materials and methods

All reagent were obtained from fluka chemicals coniucated diene hydroperoxide (CDH) levels were measured by the method descrbed by pryor and castle (10).Malondialdehyde levels were analyzed according to method described by Buege (11)

Statistical analysis:-

The data were analyzed by using student's t-test.All data were expressed as mean±SD,the over all predictire values for the results in all studied group were performed according to biostatistics by Daniel in 1987(12).

Results and Discussion:-

The role of lipid peroxidation in oxygen-induced damage to mammalian tissues has been documented for a number of species, including the human. Lipid peroxidation occurs cells with damage to the cell plasma membrane, leading to loss of cytosolic components and hence to cell 'death'. The peroxidation may be induced at high rates in the presence of Fe^{2+}. It occurs at slower rates under physiological conditions as spontaneous lipid peroxidation, which has the following characteristics. Dien conjugation (DC) and thiobituric acid reactive species (TBARS) are widely used as indicators of lipid peroxidation. DC is measure of early events of lipid peroxidation reaction where as TBARS measured end products of lipid peroxidation; MDA (13).In this work, there was significant difference in malondialdehyde (MDA) levels between diabetic patient type II and controls $p<0.01$, table (1), figure (1) were [(1.88±0.16µmol/l male, 1.92±0.23 µmol/l female)] than control group [(0.91±0.32 µmol/l male, 1.1±0.26 µmol/l female)]

Table (1): MAD (µmol/l) levels in serum of patient and healthy control

	Sex	Mean±SD	Pvalue	Sign
Patient	Male	1.88±0.16	0.001	sign
	Female	1.92±0.23	0.001	sign
Control	Male	0.91±0.32	—	—
	Female	1.1±0.26	—	—

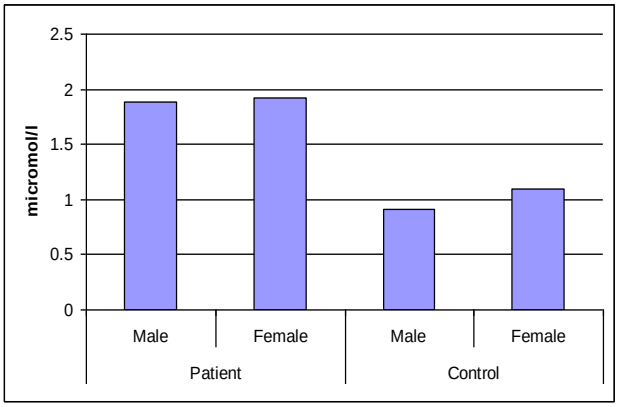

Fig (1): MAD (µmol/l) levels in serum of patient and healthy control.

Human tissues are highly susceptible to ROS-induced damage due to the high percentage of poly unsaturated fatty acids (PUFA) in the membrane. Oxidation of these PUFA can lead to decreased fluidity and flexibility of the cell membrane. Cell membranes have long been known as efficient producers of ROS. ROS such as superoxide anion ($O^{\bullet 2-}$), hydrogen peroxide (H_2O_2), and the hydroxyl ($HO^{\bullet -}$) radical are formed as byproducts of aerobic cellular processes. While under normal conditions ROS are essential for various cell membrane specific physiological processes, when produced in larger than normal quantities ROS are associated with pathogenesis of various diseases. Therefore MAD levels in patients with type II are higher than control, elevated levels of lipid peroxidation products in serum of diabetic subject and rats have been show in several studies (14, 15, 16, and 17).The results of this study indicated that serum MAD levels are elevated in diabetic patients. Higher levels of MAD are associated with reduced of antioxidant activity and increased oxidative stress (18, 19).

Increment of CDH in body fluid has been used as one of the biological markers for monitoring oxidative stress in humans. There was significant difference in CDH levels between diabetic patient type II and controls , table (2), figure (2) $p<0.01$,were[(16.1 ±2.24 µmol/l male, 15.6 ±2.37µmol/l female)]than control group [(9.4±2.3 µmol/l male, 9.51±2.4 µmol/l female)]

Table (2): CDH (µmol/l) levels in serum of patient and healthy controls

	Sex	Mean±SD	Pvalue	Sign
Patient	Male	16.1±2.24	0.001	sign
	Female	15.6±2.37	0.001	sign
Control	Male	9.4±2.3	—	—
	Female	9.51±2.4	—	—

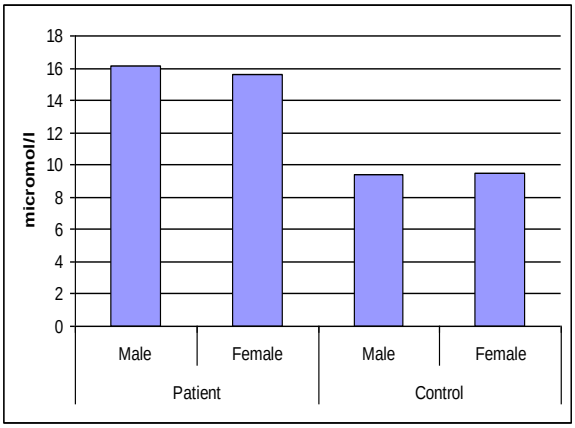

Fig (2): CDH (µmol/l) levels in serum of patient and healthy control.

Elevated levels of conjugated diene hydroperoxide could beyond to several cause; the first, decrease Gpx activity in patients which due to increased H_2O_2 production and consume antioxidants, H_2O_2 is metabolized by Gpx and glutathione reductase (GSH Reductase). The second cause to Elevated levels of conjugated diene hydroperoxide is decreased vitamin A and vitamin C concentration in serum of patients. Benzie and Strain reported the stoichiometric factors of each antioxidant (e.g. vitamin C, vitamin A, and α-tocopherol) using an FRAP assay, and demonstrated that the FRAP values were highly correlated with these antioxidant concentrations. These results suggest that the decrease of plasma vitamin C and vitamin A induced the Elevated levels of conjugated diene hydroperoxide in this study. (20)Elevated level of CDH might increase susceptibility of diabetic patients to cardiovascular complication. Elevated levels of CDH seen in diabetic patient type2 are clear manifestation of excessive formation of free radicals resulting in tissue damage (21)

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العلاقة بين الناتج الاولي والناتج النهائي لاكسدة الدهون في مصل مرضى السكري نوع 2

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الخلاصة:-

يتضمن هذا البحث مقارنة لبعض المتغيرات الكيميوحيوية المهمة عند المرضى المصابين بمرض السكري من النوع الثاني. تم الحصول على عينات الدم (30) عينة من المرضى المصابين بمرض السكري النوع الثاني(15 ذكور،15 اناث) و(30)عينة مجموعة السيطرة(15ذكور،15 اناث). تتراوح اعمار المجاميع المدروسة بين(36-46) سنة من مستشفى الديوانية العام .حيث وجدت فروقات معنوية $p<0.01$ في مستويات المالون داي الهايد (MDA) بين المرضى المصابين بمرض السكري النوع الثاني ومجموعة السيطرة [(1.88±0.01µmol/l ذكور و1.92±0.2301µmol/l اناث)] مقارنة مع مجموعة السيطرة [(0.91±0.32µmol/l ذكور و1.1±0.261µmol/l اناث)] وفروقات معنوية $p<0.01$ في مستوى الناتج الاولي CDH بين المصابين بمرض السكري النوع الثاني ومجموعة السيطرة [(16.1±2.24µmol/l ذكور و15.6±2.37µmol/l اناث)] مقارنة مع مجموعة السيطرة [(9.4±2.3µmol/l ذكور و9.51±2.4µmol/l اناث)]