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Evaluation of Superoxide Dismutase and their association with Diabetic neruopathy and Heart disease in Iraq populations

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ABSTRACT:

Complications of diabetes mellitus include both micro vascular and macro vascular complications. Diabetes mellitus causes diabetic neuropathy due to elevated blood glucose levels. High oxidant levels in diabetes complications are linked to oxidative stress, with reactive oxygen species (ROS) being a major oxidant. Endogenous antioxidants, such as SODs, are crucial for protecting cells and can be involved in cardiovascular diseases. The purpose of this study is to assess the levels of enzymatic Superoxide Dismutase in patient sera. Ninety persons were subdivided into two groups included in this study (25 patients with Diabetic neuropathy and 25 patients Heart disease), and 40 healthy subjects as a control group with range age of 30-60 years old. The enzymatic antioxidants of superoxide dismutase SOD levels were measured by enzyme linked immunosorbent assay (ELISA) method. The findings showed that the patient group's levels of lipid profile, urea, creatinine, ESR, and SOD were considerably higher than those of the control group ($p<0.05$). When diabetic neuropathy disease is present, the production of free radicals rises along with the SOD level. These antioxidants are thought to be useful markers for assessing the degree of oxidative stress in heart disease and diabetic neuropathy. Additionally, employ them as indicators for the early identification of heart disease and diabetic neuropathy. Analysis of the Receiver Operating Characteristic (ROC) curve revealed that SOD is a reliable indicator for the diagnosis of heart disease and diabetic neuropathy.

Key words: Serum blood, superoxide dismutase SOD, Lipid profile Diabetic neuropathy, heart disease.

INTRODUCTION:

Complications of diabetes mellitus include both micro vascular and macro vascular complications (Ibrahim et al., 2020, - Mohammed et al., 2024). Diabetic neuropathy, retinopathy, and nephropathy are represented the major micro vascular complications that induced by hyperglycemia, hypertension, and dyslipidemia (Hamid et al., 2021, Balaky and Kakey, 2021, Ghudhaib, 2018, Aneed et al., 2024). One common diabetic

consequence that arises from hyperglycemia and long-term diabetes is diabetic neuropathy (DN). Diabetic peripheral neuropathy (DPN) and diabetic autonomic neuropathy (DAN) are the two categories under which it falls. DPN is regarded as a clinical condition affecting the peripheral nerves, which are divided into two groups: sensory and motor neurons (Zeng et al., 2017). Additionally, diabetic sensory neuropathy was separated into other secondary kinds based on its symptoms, which can be either positive or negative. After 25 years of diabetes, diabetic neuropathy is more common in persons with the disease, particularly those with poor glycemic control (D'Amato et al., 2016). In diabetes mellitus, metabolic pathways such as mitochondrial, enzymatic, and non-enzymatic pathways are thought to be the primary causes of oxidative stress. Damage to blood vessels, enzymes, and enhanced insulin resistance may be primarily caused by lipid peroxidation, protein glycation, and glucose oxidation (Mohammed et al., 2018). Chemicals known as antioxidants, which can be either enzymes or non-enzyme biochemical compounds, are found in trace amounts and prevent oxidation. They also block the oxidative pathways that lead to progressive diseases and are linked to oxidative stress in diabetes patients (Shinde et al., 2012, Mahmood et al., 2016).

Vascular heart disease (VHD) is a serious disease and one of the major health problems that can affect elderly people often (Al-Hussona and Ahmed, 2019). The valves defects leads to weakening of the heart and the inability of to pump blood around, therefore; these defects sometimes present due to the closure or damage of one or more of the four heart valves, such as: aortic, mitral, pulmonary and tricuspid (Kabata et al., 2018). The mitral and aortic valves are the most frequently affected by vascular heart disease. Unfortunately, the valves problem can occur for various reasons, including: congenital defects at childbirth while others may be gained later in life like, aging leads to degenerate of heart valve tissue, obstruction of valves as a result of the accumulation of high fats in the blood such as: high cholesterol as well as acquired obstruction occurs due to impaired heart function (Zoriæ et al., 2019). In addition, several significant risk factors may leads to VHD including: Age, gender, hypercholesterolemia, smoking, rheumatic heart disease, diabetes and hypertension (Ma et al., 2018, Mohammed 2024).

This study looks at the levels of superoxide dismutase (SOD) enzymatic antioxidants in the blood serum of Iraqi patients with heart disease and diabetic neuropathy as chemical indicators that may remain utilized for initial illness diagnosis.

MATERIALS AND METHODS:

Venous blood samples were obtained from 25 patients with diabetic neuropathy and 25 patients with heart disease who were treated at the Baghdad Teaching Hospital in Medical City, as well as 40 individuals who served as a control group between March and April 2024. All subjects were between the ages of 30 and 60. Each sample consisted of 5 ml of venous blood collected in a gel tube and centrifuged for 10 minutes at 4000 rpm. An Eppendorf tube was used to hold the serum. The remainder were kept at -20°C to estimate SOD, which was assessed using an enzyme-linked immunosorbent test (ELISA) kit made by Aviva Systems Biology in the United States.

Statistical analysis:

SPSS 24 program was applied in this study. ANOVA test was used for determined the significant differences in the case of two groups. Correlation coefficient (r) was determined between two

variables. Also, ROC curve analysis was applied in this work to knowledge the best parameter among the studied parameters for achieve the optimal diagnosis of the case under investigation.

RESULTS:

The demographic appearances of patients and control focuses are shown in table (1). Allowing to age, the mean age of patients with neruo was 31.17 ± 8.49 years old, 29.86 ± 8.50 years old for patients with heart, and that of control subjects was 36.40 ± 11.17 years old and there was significant difference between different groups (P = 0.015). Regarding to BMI, both groups of patients showed a significant increase (p< 0.001) compared to control groups (28.88 ± 3.49 and 28.45 ± 3.53) vs (26.78 ± 2.96) respectively, whereas non-significant difference (p>0.05) was found between patient groups themselves. Furthermore, Erythrocyte Sedimentation Rate (ESR) levels in patients with neruo and patients with heart, (56.26 ± 8.96 mm/h, 48.22 ± 5.42 mm/h) respectively, were higher than healthy control subjects (5.14 ± 1.21 mm/h, P < 0.001). Serum SOD concentrations in patients with neruo were significantly greater than in patients with heart, or healthy control subjects (34.45 ± 9.77, 48.44 ± 13.92 and 75.79 ± 14.75), respectively, P < 0.001).

Table 1: SOD level measurements and clinical data of the studied groups.

Characteristic	NERUO (n=25)	HARET (n=25)	Healthy Control (n=40)	*P*
Age (years)	31.17 ± 8.49^{A}	29.86 ± 8.50^{A}	36.40± 11.17^{B}	0.015
BMI kg/m2	28.88 ± 3.49^{A}	28.45 ± 3.53^{A}	26.78 ± 2.96^{B}	0.032
Duration of disease	5.83 ± 1.64	3.65 ± 2.25		> 0.001
Cho mg/dl	208.10±21.38^{A}	203.0±16.27^{A}	164.21 ± 19.66^{B}	> 0.001
TG mg/dl	201.97 ± 10.13^{A}	186.37 ± 11.39^{A}	110.41 ± 12.43^{B}	> 0.001
HDL mg/dl	35.63 ± 3.92^{A}	40.72 ±2.95^{B}	42.98 ± 7.84^{C}	> 0.001
LDL mg/dl	113.43 ± 12.20^{A}	109.80 ± 11.64^{A}	98.84 ± 16.19^{B}	0.007
Urea mg/dl	58.76 ± 7.56^{A}	32.16 ± 4.02^{B}	24.35 ± 7.12^{C}	> 0.001
Creatinine mg/dl	1.87 ± 0.458^{A}	0.87 ± 0.166^{B}	0.76 ± 0.28^{B}	> 0.001
ESR mm/h	56.26 ± 8.96^{A}	48.22 ± 5.42^{B}	5.14 ± 1.21^{C}	> 0.001
SOD (U\L)	34.45 ± 9.77^{A}	48.44 ± 13.92^{B}	75.79 ± 14.75^{C}	> 0.001
Different latters denote to the significant differences at p< 0.05				

Correlation between serum SOD levels and other parameters

Tables (2) displayed the relationships between serum SOD levels and other indicators in individuals with heart and neurological conditions. According to the current findings, there is a substantial relationship between SOD and serum creatinine in neruo patients. However, the current findings indicate that there is no significant relationship between SOD and any other parameter in either patient group.

Table 2: shows correlation among SOD and the studied parameters

Characteristic	SOD level			
	Neruo		heart	
	r	*P*	*r*	*P*
BMI	0.076	0.718	0.106	0.578
Cho	0.038	0.855	0.110	0.501
TG	0.027	0.824	0.025	0.946
HDL	0.124	0.518	0.229	0.255
LDL	0.013	0.951	0.213	0.273
Urea	0.334	0.090	0.188	0.323
Creatinine	0.405	0.027*	0.206	0.278
ESR	0.051	0.753	0.097	0.659

r=correlation coefficient*=consider difference

Diagnostic accuracy of serum SOD

Table 3 showed the ROC curve analysis data of SOD which are including area under the curve and cut of value together with specificity and sensitivity of SOD.

Table3: ROC curve analysis data of SOD in two groups

Variables	AUC	P-value	CV	Specificity	Sensitivity
neruo group	0.846	0.001	254.36	78%	85%
Heart group	0.812	0.001	247.1	71%	80%

AUC: area under curve, CV: cut of value (U\L).

DISCUSSION:

In diabetes, oxidative stress is essential for the emergence of microvascular and cardiovascular problems. SOD, or superoxide dismutase, is a crucial antioxidant enzyme. Humans include three different types of SOD: extracellular (EC)-SOD, manganese (Mn)-SOD, and copper/zinc (Cu/Zn)-SOD. According to the literature study, SOD has been linked to problems from diabetes. (Gómez-Marcos et al.2016) discovered that Cu/Zn-SOD positively correlated with plasma uric acid and triglycerides, while negatively correlated with pulse pressure, arterial stiffness index, and HDL cholesterol (Gómez-Marcos et al., 2016). In Chinese patients, serum EC-SOD activity was linked to the advancement of type 2 diabetes and was an independent risk factor for DR (Zhao et al., 2018).

According to Table (1) findings, there were non-significant ($p>0.05$) variations in the patients' and control groups' ages and BMIs, respectively. Other research concurs with this finding (Mahmood et al., 2013; Kamran M et al., 2016). As indicated in Table 1, there are notable variations in the urea and creatinine levels in the patient and control groups at the similar period. This finding contradicts earlier research (Ghudhib et al., 2018, Mohammed et al., 2018). The authors of the US guidelines on obesity came to the conclusion that higher BMI levels were linked to a higher risk of both fatal and nonfatal coronary heart disease in overweight and obese adults after conducting a systematic evaluation of the literature (Atique et al., 2016). Table 2's findings indicated that the sick group's SOD levels were significantly higher than those of the control group. These findings contradict those

of recent research that reported a reduction in endogenous antioxidants in diabetic conditions (Mesaros et al., 2012, Dincer et al., 2002). In the same manner, levels of ESR are significant increase in patients group compared with control group. Superoxide dismutase (SOD), a natural antioxidant enzyme, acts as a defense against free radicals, reducing diabetic complications when endogenous antioxidant levels are elevated (Bala and Haldar 2013, Catanzaroa et al., 2013, Surai and Fisinin, 2014). Significant variations in SOD were also revealed by the ROC curve analysis results in this study. SOD shields the heart from oxidant-induced fibrosis, apoptosis, and function loss and is essential for proper cardiac morphology (Kliment et al., 2009). SOD has been suggested as a promising therapeutic target for DR because it can rectify the imbalance between ROSs and antioxidant scavengers and downstream consequences (Ikelle et al., 2019). It was discovered that SOD plays a protective function in the demise of retinal capillary cells and, eventually, in the pathophysiology of DR (Kowluru et al., 2006). Our research and all of these others show a strong correlation between SOD and long-term consequences from diabetes. In physical replicas, elimination of SOD in transgenic diabetic mice protects or accelerates cardiomyopathy (Mao et al., 2019), diabetic retinopathy (DR) (Zhaoliang et al., 2021), and nephropathy (De Blasio et al., 2017). However, data from clinical practice are subject to numerous confounding circumstances. This suggested that SOD is a preventative measure against complications from diabetes. It's interesting to note that SOD was only linked to cardiovascular problems associated with chronic diabetes in males, not women. Previous research did not show sexual dimorphism in this association. According to the research, patients without diabetes also showed sex variations in the connection between SOD and AS (Han et al., 2018).

Furthermore, the metabolic syndrome and other atherosclerosis risk factors, including diabetes, dyslipidemia, hypertension, and obesity, is linked to oxidative stress (Hopps et al., 2010). In individuals with cardiac disease, the probability of death is predicted by biomarkers of oxidative stress (Heslop et al., 2010). It has been demonstrated that oxidative stress contributes to the early vascular morbidity and death in diabetics (Doney et al., 2005). Oxidative stress is implicated in cardiovascular morbidity and mortality associated with diabetes, according to studies conducted in animal models (Stull et al., 2004, Yan-Jun et al., 2020).

SODs and other antioxidant enzymes scavenge reactive oxygen species (ROS) and prevent the vascular wall from degrading NO (Faraci FM, Didion SP 2004). Smooth muscle cells manufacture and secrete EC-SOD to the extracellular space, which is seen in high concentrations in the vascular wall (Kamel et al., 2015).

CONCLUSION:

Heart disease and diabetic neuropathy enhance the production of free radicals, which lowers endogenous antioxidants like SOD. In diabetic neuropathy and heart disease, this biochemical parameter is thought to be a useful indication of oxidative stress, and it may be utilized as a marker for the early diagnosis of diabetes problems. This assumption is supported by the use of Receiver Operating Characteristic (ROC) curve analysis. The strongest sign for illness diagnosis, according to the results of ROC curve analysis, is the SOD level.

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Conflicts of Interest Statement……

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