

Evaluation of Acetylcholinesterase, Dopamine, IL-6, and Antioxidant Biomarkers in Patients with Parkinson's Disease

Qaisar Mashan Abd

Department of Chemistry, College of Education of Pure Science, University of Tikrit, Iraq

ABSTRACT

Background: Parkinson's disease (PD) is a progressive neurodegenerative movement disorder characterized by bradykinesia, rigidity, and tremor. Laboratory investigation of neurotransmitters, cytokines, and oxidative stress markers may provide important insights into its underlying pathophysiology. **Methods:** This case-control study included 30 patients with clinically diagnosed PD (aged 45–65 years) recruited between May and December 2024 from the Medical City, and 20 age-matched healthy controls. Following venous blood collection (5 mL), serum samples were obtained by centrifugation and analyzed for acetylcholinesterase activity, dopamine concentration, interleukin-6 (IL-6), and antioxidant biomarkers including glutathione (GSH) and malondialdehyde (MDA). **Results:** Compared with healthy controls, patients with PD showed significantly elevated serum acetylcholinesterase, IL-6, and MDA levels ($p < 0.05$). In contrast, dopamine and GSH concentrations were significantly reduced in PD patients ($p < 0.05$). **Conclusion:** Alterations in acetylcholinesterase, dopamine, IL-6, and antioxidant markers highlight the role of both neuroinflammation and oxidative stress in the pathology of PD. These biomarkers may serve as potential laboratory indicators for disease progression and therapeutic monitoring.

Keywords: Parkinson's Disease, Acetylcholinesterase, Dopamine, IL-6, Oxidative Stress, Biomarkers

INTRODUCTION

Parkinson's disease (PD) is a group of progressive neurodegenerative disorders, affecting approximately 6 million people worldwide and nearly 1% of the population over 60 years of age. The hallmark of PD is the progressive degeneration of dopaminergic neurons in the substantia nigra, resulting in dopamine deficiency within the basal ganglia, the brain region responsible for regulating motor control. Clinically, PD presents with tremor, rigidity, bradykinesia, and postural instability, symptoms that may overlap with other neurological conditions, thereby complicating early diagnosis[1]. Dopamine plays a central role in transmitting nerve signals related to motor function. Reduced dopamine levels are a defining feature of PD, making it a critical biomarker for both disease onset and progression. However, additional biochemical factors contribute to the complex pathophysiology of PD [2, 3]. Among these, acetylcholinesterase (AChE), an enzyme regulating the neurotransmitter acetylcholine at neuromuscular junctions, has been implicated in neuronal function and may provide insights into cholinergic alterations in PD. Its plasma analog, butyrylcholinesterase (BChE), synthesized in the liver, also plays a role in neurodegeneration, though its function is less defined [4]. Oxidative stress is another central mechanism in PD pathology. Glutathione (GSH), a key intracellular antioxidant, regulates protein stability, cell signaling, and redox homeostasis. Its depletion has been linked to neurodegenerative diseases including PD, as well as systemic disorders such as type 2 diabetes and cardiovascular disease. Malondialdehyde (MDA), a reactive byproduct of lipid peroxidation, serves as a toxic marker of oxidative damage by interacting with proteins and DNA, exacerbating cellular stress[5]. Furthermore, inflammatory mediators such as interleukin-6 (IL-6) are increasingly recognized as contributors to PD progression, bridging neuroinflammation and oxidative stress. Together, these parameters — dopamine, AChE, IL-6,

GSH, and MDA — provide a panel of laboratory biomarkers that may enhance diagnostic sensitivity and support monitoring of disease progression[6]. The present study evaluates serum levels of acetylcholinesterase, dopamine, IL-6, GSH, and MDA in patients with PD compared to healthy controls, aiming to clarify their potential diagnostic and prognostic significance[7, 8]. Glutathione is an abundant low molecular-weight thiol within cells and body tissues. It plays an essential role in many cellular processes, such as its work as an antioxidant and its role in regulating protein function and stability, gene expression, cell proliferation, and regulating signals between cells [9]. Glutathione is linked to many diseases, including type 2 diabetes [10], heart disease [11], and PD [12, 13].

Collection of Blood

The samples were from medical laboratories in the Medical City after the patients were diagnosed by the doctor through clinical symptoms that are characterized by (tremors, muscle stiffness, slow movements, loss of spontaneous movements, dementia, and changes in speech). The study sampled 30 patients with PD (45-65 years of age) (1/5/2024 to 20/12/2024): 20 from healthy people (as a control group) and 5 ml from patients and the controls separated using a centrifuge to get the serum, then Acetylcholine esterase, Dopamine, Interleukin 6 -IL-6, and some antioxidants such as glutathione-GSH, malondialdehyde-MDA.

Estimation the Concentration of Acetylcholine Esterase, Dopamine, and IL-6 in Blood Serum

The concentration of (acetylcholine esterase, dopamine, and IL-6) in sera were determined based on several kits from Elabsience an American company.

Determining Antioxidants in Sera

The present study also determined serum glutathione-GSH by Elman's reagent in the modified method [14]. The level of malone dialdehyde was measured by the researcher Guidet [15].

Statistical Analysis

The statistical analysis of the collected data was carried out using the Statistical Package for the Social Sciences (SPSS) software. Descriptive statistics were applied to calculate the mean values along with their corresponding standard deviations (Mean $\pm$ S.D.) in order to provide a clear understanding of the central tendency and variability

within the study groups. In addition, comparative analyses were conducted to evaluate potential differences between the patient and control groups with respect to the biochemical and clinical parameters under investigation.

The level of statistical significance was set at a probability value of $P \geq 0.05$, which was considered sufficient to determine whether the observed differences occurred by chance or reflected meaningful variations. This approach allowed for a robust assessment of the relationship between triglycerides, insulin resistance, and other associated metabolic indicators in patients with type 2 diabetes mellitus.

Results

Determining Acetylcholine Esterase, Dopamine, and IL-6, GSH, MDA in all Groups

Table 1: The Mean $\pm$ SD of Parameters in all Groups

Groups	Mean $\pm$ SD		P-Value
Variables	Control	Patients	
ACH (pg/ml)	21.735 $\pm$ 4.038	40.134 $\pm$ 6.787	<0.0001*
Dopamine (pg/ml)	885.546 $\pm$ 186.429	517.259 $\pm$ 203.279	<0.0001*
IL-6 (pg/ml)	17.992 $\pm$ 5.751	39.240 $\pm$ 6.521	<0.0001*
GSH (μ g/ml)	6.612 $\pm$ 1.402	3.621 $\pm$ 1.647	<0.0001*
MDA (ng/ml)	9.839 $\pm$ 2.478	24.733 $\pm$ 11.962	<0.0001*

$P \leq 0.05$

Acetylcholine esterase, IL-6, and MDA significantly rose and Dopamine, and GSH) in patients with PD significantly.

Decreased in relation to the controls at $P \leq 0.05$. as in fig (1,2, 3,4,5).

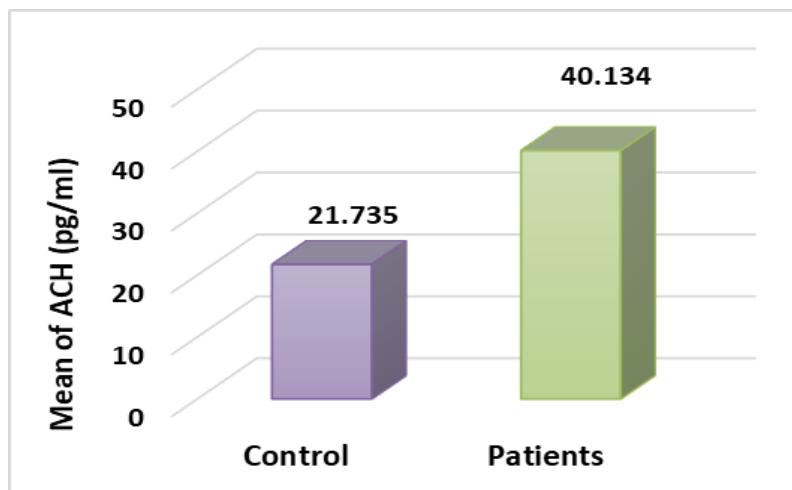


Figure 1: Levels of ACH in all Groups

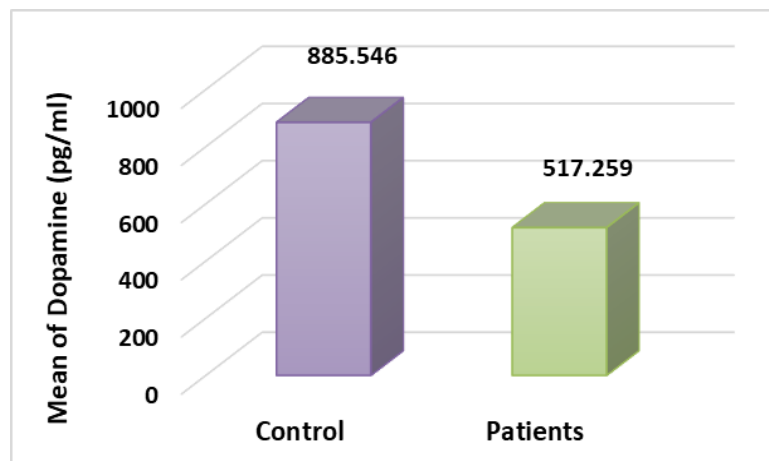


Figure 2: Levels of Dopamine in all Groups

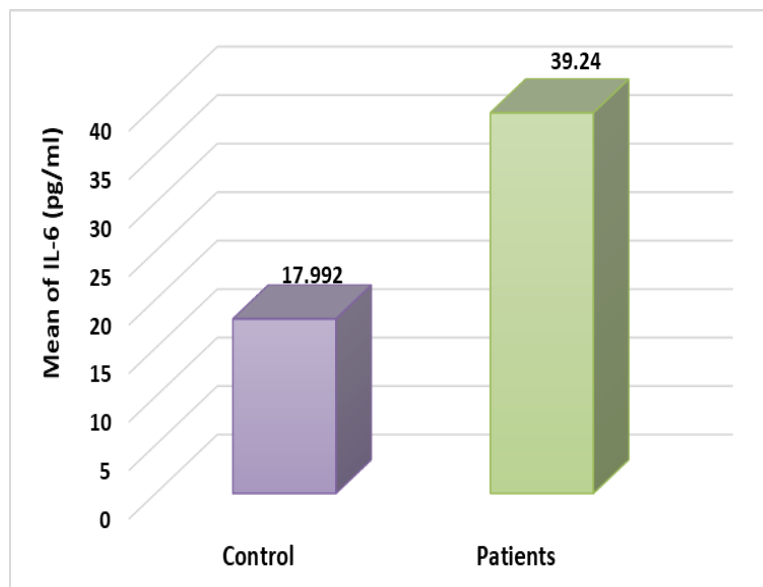


FIGURE 3: Levels of IL-6 in all Groups

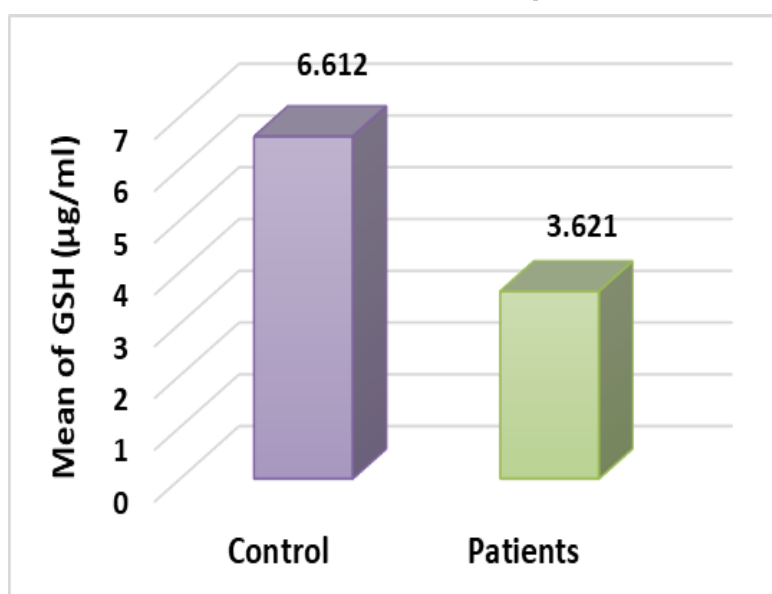


FIGURE 4: Levels of GSH in all Groups

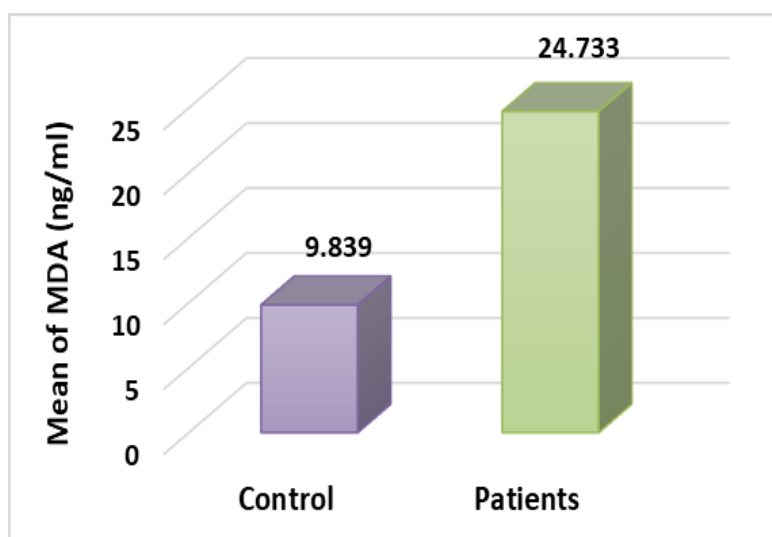


FIGURE 5: Levels of MDA in all Groups

ROC Curve for all Parameters in Blood Serum of all Groups

Table (2) reveals the area beneath the curve for the variables studied in the current research. (ACH, dopamine, IL-6, GSH, IL-6) for the group of patients and healthy controls. The findings revealed that the area under the curve's (AUC) value for ACH, dopamine, IL-6, GSH,

MDA was (0.993), (0.927), (1.000), (0.7844), (0.972) respectively, and the sensitivity was (100.00), (87.50), (100.00), (82.61), (91.67), respectively while the specificity was (91.67), (87.50), (100.00), (95.83), (95.83) respectively at the probability level ($P < 0.01$) for the two groups of patients and healthy ones, as in the figure (6,7,8).

Table 2: The Area Under the Curve for the Variables Under Consideration

Variables	AUC	Cut Off	Sensitivity %	Specificity %	Accuracy	P-Value
IL-6	1.000	>27.391	100.00	100.00	1.0000	<0.0001
ACH	0.993	>25.768	100.00	91.67	0.9167	<0.0001
Dopamine	0.927	≤707.198	87.50	87.50	0.7500	<0.0001
GSH	0.7844	≤4.733	82.61	95.83	0.7844	<0.0001
MDA	0.972	>13.218	91.67	95.83	0.8750	<0.0001

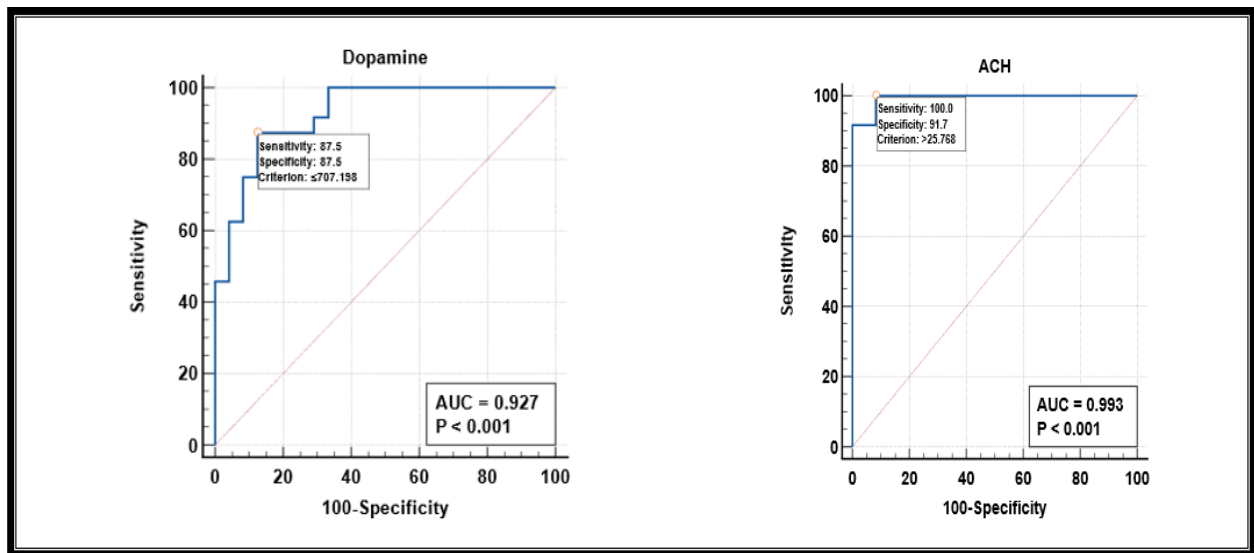


Figure 6: ROC Curve of ACH and Dopamine in all Groups

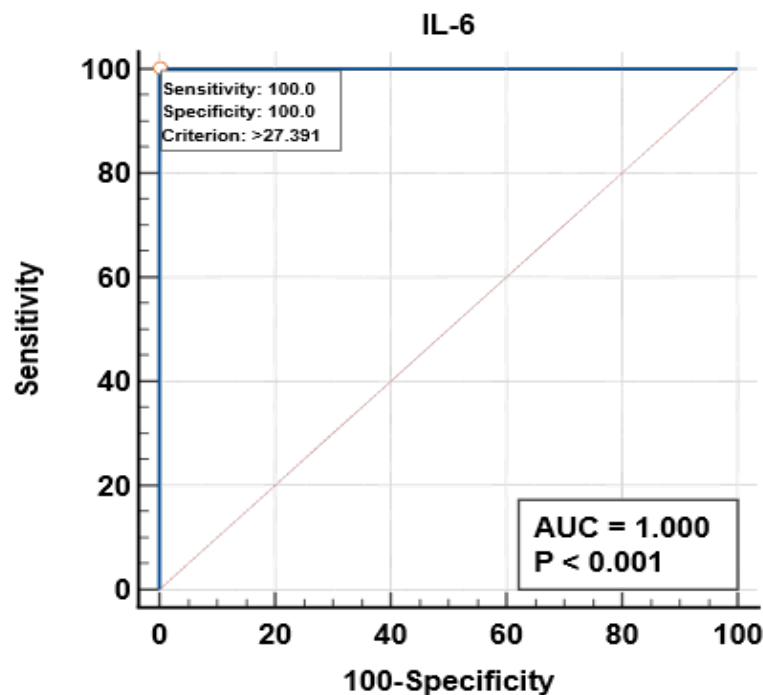


Figure 7: ROC Curve of IL-6 in all Groups

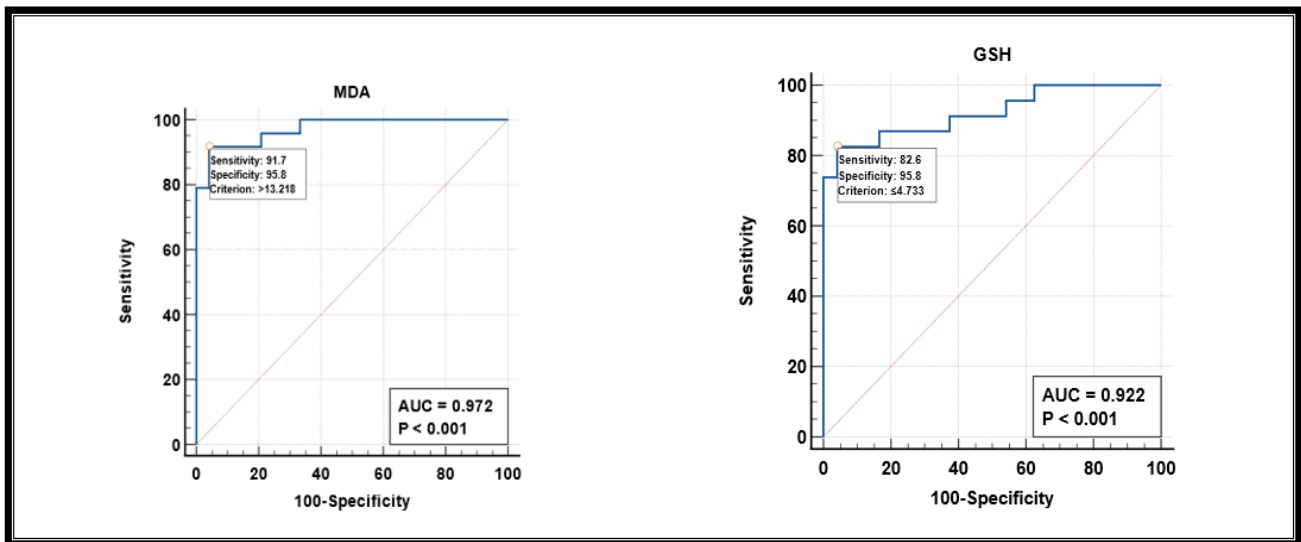


Figure 8: ROC Curve of GSH and MDA in all Groups

In this study, the area under the curve, sensitivity, and specificity were good for all variables studied, especially interleukin 6, as these variables can be considered important diagnostic variables for predicting PD.

Discussion

The activity of the enzyme acetylcholinesterase in the blood serum of Parkinson's patients significantly increased relative to the healthy group. PD is a movement disorder of a wide range of non-motor symptoms associated with non-dopaminergic pathways. Since dopamine depletion, anticholinergic medications treat the disease, so cholinesterase inhibitors may progress cognitive function and decrease symptoms in patients with PD [16]. Psychotic symptoms significantly increase the burden, and cholinesterase inhibitors could effectually treat psychotic symptoms in these disorders [17]. Neuroimaging, immunohistochemical, and radiological identification of effector cells and pathways is based on effector cell expression of acetylcholine synthesis and its deletion. Acetylcholine is synthesized by the choline acetylation by the cytosolic enzyme choline acetyltransferase and then pumped to synaptic vesicles using vesicular acetylcholine transporters. Therefore, the cholinesterase enzyme can treat PD [18]. The research results indicated lower dopamine levels in the patient group in relation to the healthy group. Dopamine level dropped in neurons to underlie motor deficits in PD. Therefore, deficits in dopamine release in PD would not happen on cell death, but when there is axonal dopamine release dysfunction or dysregulation prior to cell loss [19]. The pathological features of PD are low dopamine levels and the gradual loss of nerve cells. Disturbances in dopamine synthesis, storage, transport, and metabolism increase the neurodegeneration of dopamine neurons [20].

Interleukin-6 levels in patients with PD significantly rose. Some studies have shown a change in the concentration of inflammatory cytokines, like IL-6, in PD. Furthermore, elevated inflammatory cytokines have been linked cognitive impairment and weak physical capacity in older adults. Therefore, it was found that these patients had major problems in maintaining balance during required functional tasks, so high interleukin 6 may be involved in accelerating the process of muscle catabolism, which leads to muscle atrophy and thus

contributes to weakness and fatigue and is linked to functional disability in Parkinson's patients [21]. The current study found that interleukin 6 concentration are rise in Parkinson's patients compared to healthy people confirming some of the studies [22, 23], so interleukin 6 appears to be associated with neuronal survival and difference in the brain, so immune or inflammatory mechanisms are involved in neurodegeneration in Parkinson's patients [24]. A study [25] also indicated that patients who suffer from poor movement, lack of concentration, and memory ability and who suffer from PD were found to have high levels of interleukin 6. An increase in this vital inflammatory indicator in the blood indicates the development of non-motor weakness in patients. Yet, higher levels of interleukin-6 in Parkinson's patients and that its levels are connected to non-motor symptoms and cognitive dysfunction [26]. IL-6 may be important in the pathophysiology of non-motor conditions [27]. A study [28] has also found that genetic variants of interleukin 6 are significantly linked to the PD pathogenesis. Yet, the research indicated lower levels of glutathione and higher levels of malondialdehyde in patients with PD than the healthy. Oxidative stress is important in nigral neurons and metabolic failure of antioxidant mechanisms could theoretically making the chemical process easy causing lipid peroxidation. To clarify whether high rates of lipid peroxidation may elevate the disease in PD as in plasma levels of malondialdehyde (MDA) study in 80 patients [29]. Also, there were significant changes in the level of malondialdehyde in Parkinson's patients. A study indicated that people with PD had high levels of malondialdehyde and low levels of glutathione confirming the results with levels of malondialdehyde increase with advancing age groups. Cells in the nervous system, especially neurons, are among the cells most susceptible to oxidative damage due to their low metabolic rates, limited masticatory capacity, and high iron content [30]. Moreover, microglia and astrocytes induce ROS-mediated oxidative stress through neuroinflammatory processes [31]. Iron is widely distributed in the central nervous system, and is linked to stress. Oxidative stress and induction of cell death, especially in pathological conditions related to aging and neurodegeneration [32]. Malone dialdehyde was used in the current study indicating oxidative stress in people with PD. The results revealed a rise in the level of MDA in the serum the patients than the healthy people confirming other studies that linked the relationship Oxidative stress

causes many types of chronic neurological diseases and disorders, such as epilepsy and autism. A scientific study indicated that there is a role for abnormal mitochondrial shapes and functions as well as increased oxidative processes that cause PD [33]. Glutathione deficiency was first identified as active in causing PD in 1982 [34]. The reason is that the stages of the disease may be early, i.e. in the first stage, so consuming it as an antioxidant at low levels. The explanation for its relative decrease may be due to the high rate of oxidative stress in patients, which leads to depletion or drop in the level of glutathione as its antioxidant action, as by Mischley et al. [35] indicated that glutathione levels in the blood might serve as a vital sign for Parkinson's patients. They found that blood glutathione is the most sensitive and associated with aging, and also recorded a statistically significant association with the severity of PD, as blood glutathione recorded a decrease with increasing age. A study by Dexter et al. [36] on post-mortem Parkinson's patients showed a rise in oxidative stress and a drop in glutathione, the main antioxidant in the brain. Also, the elevated levels of malondialdehyde are directly linked with the

increase in age, and serum glutathione levels witnessed a non-significant decrease with age. This study is consistent with several studies indicating an increase in levels of malondialdehyde with age in certain pathological conditions such as parasitic infections [37, 38], and this result is supported by other studies that confirm increased fat oxidation and oxidative stress in older people [39, 40]. It was found in a study [41] that the area under the curve for the level of interleukin 6 was 0.599, and this does not agree with the results of the research, as it was found that interleukin may be important in the diagnosis of PD.

Conclusion

The level of neurotransmitters rose, including acetylcholinesterase, and that an increase in indicators of inflammatory factors and oxidative stress, including interleukin 6 and malondialdehyde, is an indicator of the occurrence of the disease, while the levels of dopamine and antioxidants also drop as a result of the worsening of the disease condition.

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