

Analysis of Differential Characteristics of Clinical-Functional Changes in Early and Prodromal Stages of Parkinson's Disease

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Abstract While instrumental methods for preclinical diagnosis of Parkinson's disease (positron emission tomography (PET), single-photon emission computed tomography, and functional magnetic resonance imaging (MRI) spectroscopy) help identify and visualize functional deficiency of specific neurons in the substantia nigra of the brain, their high cost and need for specialized equipment limit the possibility of early detection of risk groups among the healthy population, even in developed countries. Therefore, identifying specific, highly sensitive, economically effective, and easily applicable biomarkers for Parkinson's disease is a crucial task for early diagnosis and treatment of this condition.

Keywords Positron emission tomography, Functional magnetic resonance imaging, Parkinson's disease

1. Introduction

Parkinson's disease (PD) is a progressive degenerative disease of the central nervous system and is considered the second most common neurodegenerative disease among the population over 65 years of age worldwide. According to the World Health Organization, more than 8.5 million people worldwide suffer from this disease [1,5]. In the Republic of Uzbekistan, the incidence rates of Parkinson's disease are increasing year by year due to the acceleration of the population aging process. As of 2023, 150-180 cases per 100,000 population were recorded in our republic, which is 2.3 times higher than 10 years ago [2,6]. Early diagnosis of Parkinson's disease is one of the most complex problems in modern neurology. Traditionally, the disease is diagnosed when motor symptoms appear, but by this time, 50-70% of dopamine neurons have already been destroyed. This significantly limits the effectiveness of early intervention and treatment [3,7]. The prodromal stage is a period that occurs 5-20 years before the appearance of motor symptoms, during which various non-motor symptoms manifest. Early detection and proper analysis of these symptoms are of great importance in developing strategies for early diagnosis and treatment of the disease [4,8].

2. Methodology

This scientific work was conducted by the Department of Neurology of Bukhara State Medical Institute at the Bukhara District Medical Association. A total of 216 patients were studied to achieve the goals and objectives of the research. All patients were divided into 2 groups. A total of 246 individuals were involved in the study, divided into the following groups:

- Group I – 176 patients in the clinical stage of Parkinson's disease;
- Group II – 40 individuals with prodromal symptoms belonging to the high-risk group (clinically PD not formally diagnosed, but having characteristic features);
- Group III – 30 age- and sex-matched, functionally healthy control subjects.

Inclusion Criteria:

- Patient consent to participate in the study
- Presence of parkinsonism syndrome
- Availability of MRI results

Exclusion Criteria:

- Acute course of comorbid diseases
- Taking neuroleptics
- Presence of kidney or heart failure in decompensation stage

Demographic Characteristics

Group 1 included 175 patients, of which 78 (68.42±4.35%) were men and 97 (74.05±3.83%) were women. Although the number of women was relatively higher in the gender distribution, this difference was not statistically significant according to chi-square analysis ($\chi^2=2.063$; $p=0.151$).

Group 2 included 19 men (16.67±3.49%) and 21 women (16.03±3.21%), with proportional and non-significant gender composition differences ($\chi^2=0.100$; $p=0.752$).

Group 3 (control group) included 17 men (14.91±3.34%) and 13 women (9.92±2.61%). This group also showed no statistically significant gender distribution differences ($\chi^2=0.533$; $p=0.465$).

The Pearson χ^2 analysis result ($\chi^2=1.524$; $p=0.467$) for overall gender distribution confirms that gender balance was maintained among the study groups.

Age analysis showed: Group 1 had an average age of 60.22±0.69 years, Group 2 had 58.78±1.17 years, and Group 3 had 59.67±1.28 years. Patient ages were nearly identical across all groups and statistically non-significant (Table 1).

Table 1. Distribution of Patients by Groups and Gender

Groups	Gender		Chi-square	Age
	Male	Female		
	abs	M±m,%		
Group 1	78	68.42±4.35	97	74.05±3.83
Group 2	19	16.67±3.49	21	16.03±3.21
Group 3 (Control)	17	14.91±3.34	13	9.92±2.61
P	Pearson $\chi^2 = 1.524$; $p = 0.467$			

Note: * - compared to control group (** - $P<0.05$; *** - $P<0.01$; * - $P<0.001$); Δ - compared to "Group 1" (Δ - $P<0.05$; $\Delta\Delta$ - $P<0.01$; $\Delta\Delta\Delta$ - $P<0.001$) reliable differences between arithmetic mean values are indicated.*

3. Results

At the center of neurodegenerative processes in Parkinson's disease is oxidative stress, namely the imbalance between free radicals and antioxidant defense mechanisms. Therefore, assessing redox balance has decisive scientific and clinical significance for deep understanding of the metabolic foundations of this pathological process, proper determination of therapeutic strategies, and evaluation of treatment effectiveness.

The main biochemical indicators of redox balance in the study groups were analyzed before treatment (Table 2). This analysis allowed assessment of oxidative stress levels and the functional state of the antioxidant defense system.

Malondialdehyde (MDA) - as the main marker of lipid peroxidation, was detected at levels of 5.51±0.04 $\mu\text{mol/L}$ in Group 1, 4.57±0.07 $\mu\text{mol/L}$ in Group 2, and 3.27±0.06 $\mu\text{mol/L}$ in the control group. MDA levels were significantly higher in the study groups compared to the control group, indicating pathogenic mechanisms associated with oxidative stress in the disease. Additionally, MDA levels in Group 2 patients were lower compared to Group 1, suggesting relatively lower stress levels.

Reduced glutathione levels - a key parameter of antioxidant defense, were recorded at 3.16±0.03 $\mu\text{mol/L}$ in Group 1, 4.19±0.06 $\mu\text{mol/L}$ in Group 2, and 4.98±0.07 $\mu\text{mol/L}$ in the

control group. This indicator also showed statistical differences between groups, with the significant decrease in reduced glutathione levels in Group 1 confirming the decline in antioxidant potential during the disease process.

Table 2. Biochemical Comparative Analysis of Redox Balance Indicators in Study Groups Before Treatment (M±m)

Indicators	Study Groups
	Group 1
Malondialdehyde	5.51±0.04*
Glutathione (reduced)	3.16±0.03*
Superoxide dismutase	75.29±0.78*
Glutathione peroxidase	35.09±0.36*
Catalase	25.53±0.3*
Glutathione ratio - reduced to oxidized glutathione	4.94±0.07*
8-hydroxy-2'-deoxyguanosine	10.41±0.12*
DOPAC (dopamine metabolite)	75.79±0.73*

Note: * - compared to control group (** - $P<0.05$; *** - $P<0.01$; * - $P<0.001$); Δ - compared to "Group 1" (Δ - $P<0.05$; $\Delta\Delta$ - $P<0.01$; $\Delta\Delta\Delta$ - $P<0.001$) reliable differences between arithmetic mean values are indicated.*

Superoxide dismutase (SOD) activity was 75.29±0.78 in Group 1, 92.44±1.33 in Group 2, and 118.74±1.46 units/mg protein in the control group. SOD activity decreased with reliable differences in all groups, with Group 2 showing better preservation compared to Group 1. This reflects the degree of functional deficiency in the antioxidant enzyme system.

Glutathione peroxidase and catalase activities were also recorded at the lowest levels in Group 1 (35.09±0.36 and 25.53±0.3 respectively), higher activities in Group 2 (44.69±0.88 and 29.1±0.78), and the highest levels in the control group (54.62±0.97 and 38.05±0.47). These indicators clearly demonstrate the degree of decreased antioxidant enzyme activity.

The ratio of reduced to oxidized glutathione was 4.94±0.07 in Group 1, 6.83±0.11 in Group 2, and 8.01±0.1 in the control group. This ratio is an overall integral indicator of antioxidant status, showing serious impairment in Group 1.

4. Conclusions

Thus, in the prodromal stage of Parkinson's disease, cognitive functions, smell sensation, REM sleep disorders, SCOPA-AUT indicators, and autonomic disorders identified through Ewing tests were statistically significantly detected ($p < 0.05$), which is significant for early diagnosis of the disease and important in determining screening methods. Oxidative stress indicators - malondialdehyde and 8-oxoguanosine levels were decreased, while glutathione and antioxidant enzyme (catalase, GPx) levels were increased ($p < 0.001$). This condition demonstrates the role of redox imbalance in the pathogenetic mechanism of the disease and shows its correlation with clinical symptoms.

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