

## Role in Disease Progression: Non-Motor Manifestations in Parkinson's Disease

**Daminova Khilola Maratovna**

Associate Professor, Tashkent Medical Academy, Tashkent, Uzbekistan

**Abstract:** Smell impairments occur several years before movement disorders. The results of observation of 213 patients with PD are presented. The presence of hyposmia in patients with early onset of PD is an important biomarker of the risk of future development of PD.

**Keywords:** brain, hypoasmia, anosmia.

**Introduction.** Early diagnosis of Parkinson's disease is difficult due to the similarity of clinical manifestations in the early stages with essential tremor, multiple system atrophy, progressive supranuclear palsy, etc. That is why the search for biomarkers of the neurodegenerative process in PD - biochemical, neurophysiological, neuroimaging, etc. - is currently considered extremely relevant [ 3,5]. From a pathophysiological point of view, PD is characterized by a decrease in the inhibitory influence of the pallidum on the striatum, which leads to "inhibition of inhibition" of peripheral motor neurons [ 4 ] . Olfactory impairment may be an early clinical sign of PD [1,2]. With the progression of the disease, the presence of these pathological bodies is noted in the neurons of the substantia nigra, midbrain, basal ganglia and, at the final stages, in the cells of the cerebral cortex. Primary parkinsonism includes Parkinson's disease (PD), the second most common neurodegenerative disease and a significant medical and socioeconomic problem, as well as juvenile parkinsonism. The diagnosis of the disease is made on the basis of developed clinical criteria [6,7], the correct application of which is largely determined by the qualifications of the doctor, and therefore, in the early stages of the disease, its differentiation from other forms of pathology can cause serious difficulties. Non-motor complications increase as the disease progresses. Almost all PD biomarkers are being considered for their use in diagnosing the early and premotor stages of the disease. Of great interest to neurologists is the presence of olfactory disorders in neurodegenerative diseases. PD, as already mentioned, in its earliest stages is characterized by the development of olfactory deficits. When using special olfactory tests, it turned out that the majority of PD patients have a clear olfactory dysfunction in the form of deterioration in the differentiation and identification of odors. These changes are largely "hidden" and for many years constitute the latent stage of the disease. PD, as already mentioned, in its earliest stages is characterized by the development of olfactory deficits. Olfactory disorders occur several years before movement disorders. In general, among patients with PD, olfactory disorders are detected in 70-90% of cases [8], and according to Lotsch et al. [8], even in 99% of cases. In this case, olfactory disturbances may not be felt by the patient himself, therefore, to identify them, it is important to conduct special testing.

**Purpose of the study.** Evaluation of biomarkers of the prodromal stage in Parkinson's disease and their role in disease progression.

**Materials and methods .** Under observation were 213 patients with PD, of whom 92 (43.19%) were women, 121 (56.81%) were men, whose average age was  $46.17 \pm 0.63$  years, mainly of

Uzbek nationality. Patients with PD were selected in accordance with the international criteria of the British Parkinson's Disease Society Brain Bank. To exclude other causes of parkinsonism syndrome, patients underwent CT or MRI of the brain. In patients with PD, the form of the disease (akinetic-rigid, mixed or trembling) and the functional stage of the disease (according to the Hoehn-Yahr scale) were assessed. Olfactory disorders were studied using the Sniffin Stix test (SST) from Burchard (Hamburg, Germany). All patients underwent examination of ENT organs.

**Results.** The work was carried out in several stages of observation. Based on the analysis and generalization of scientific publications of domestic and foreign researchers on the problem of predicting the outcomes of Parkinson's disease, out of 600 outpatients, 213 patients with an average age of  $46.17 \pm 0.63$  years were selected for the study. The 213 patients with PD we examined, 92 (43.19%) women, 121 (56.81%) men, were divided into two groups, group I - with early onset of PD, consisted of 79 (37.09%) patients with early onset of PD, of which 45 (56.86%) were men, and

Table 1. Distribution of patients with early onset PD and late onset PD by gender,

n = 213

With early onset of PD, n =79(37.09%)		With late onset of PD, n = 134 (62.91%)	
Group I – with early onset of PD, n =48(22.54%)	Group II – with early onset of PD and complicated SA, n =31(14.55%)	Group III – with late onset of PD, n =58 (27.23%)	I V - with late onset of PD and with aggravated SA, n = 76 (35.68%)
Men 27(56.25%)	Men 18(58.06%)	Men 32(55.17%)	Men 44(57.89%)
Women 21(43.75%)	Women 13(41.94%)	Women 26(44.83%)	Women 32(42.11%)

34 women (43.04%). There were 31 (14.55%) patients with PD with an early onset of PD, but with aggravated SA, of which 18 (58.06%) were men and 13 (41.94%) were women. Group II – with late onset of PD, consisted of 134 (62.91%) patients, of which 75 (55.97%) were men and 59 (44.03%) women. There were 76 (35.68%) patients with PD with a late onset of PD, but with aggravated SA, of which 44 (57.89%) were men and 32 (42.11%) were women. An assessment of olfactory disorders in 213 patients with PD, carried out using SST, who were divided into two groups, showed clear impairments in the study group in three indicators - threshold, discrimination, identification. The majority of examined PD patients with early onset, 58 (27.23%), revealed dysosmia in the form of hyposmia (GRI 16-29 points) and anosmia (GRI <15 points), 13 (6.10%) and normosmia 142 (66.67%). The frequency of manifestation of hyposmia is 58 (27.23%) and in early parkinsonism group I (n = 48), in men 18 (66.67%), in women 14 (66.67%); I I group (n = 31), early parkinsonism, but with SA, hyposmia was detected in 15 (83.3%) men, 11 (84.62%) in women. It was revealed that with late onset I I I group and I V group SA indicators, that is, anosmia, and with early parkinsonism I I I group, in men 9 (33.3%), in women 7 (33.3%); I I group, early parkinsonism, but with SA, anosmia was detected in 3 (16.67%) men and 2 (15.38%) in women. It was revealed that in the late onset of group I I I and group I V SA, anosmia was not detected.

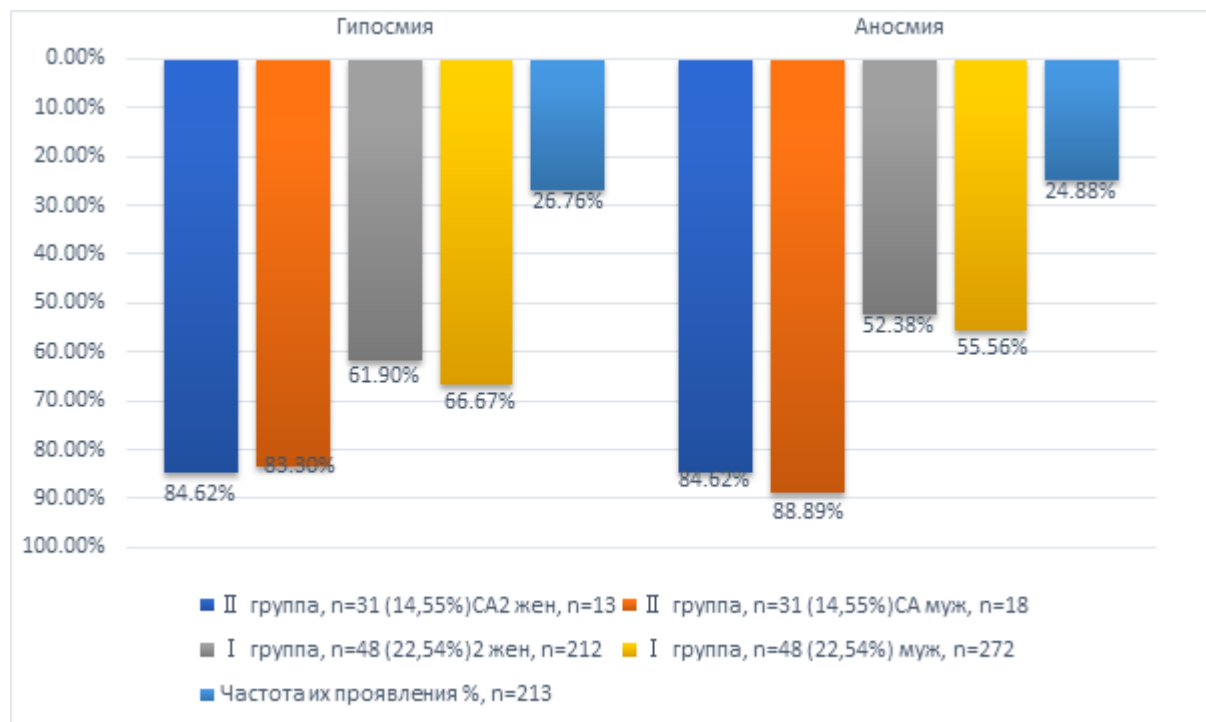


Fig.1. Level of olfactory disorders in early parkinsonism, n =79

**Discussion.** At early onset, out of 79 patients, 8 (10.13%) had a normal level of smell according to three indicators, and with early parkinsonism, group I, in men 3 (11.11%), in women 2 (9.52%); I I group, early parkinsonism, but with AS, a normal level of smell was found in 2 men (11.11%), and in women 1 (7.69%). In 58 cases (73.42%), the sense of smell was reduced in all studied indicators at an early onset. With late parkinsonism, 134 (62.91%) had a normal level of smell according to three indicators, with early onset in 8 (10.13%), thus normosmia in our patients was detected in 142 (66.67%) patients.

In the majority of the examined PD patients, 185 (86.85%) were found to have dysosmia in the form of hyposmia (OI 16-29 points) and anosmia (OI <15 points), normosmia 28 (13.15%), 163 (76.53%) hyposmia and 22(10.33%) anosmia. Of the 213 patients, 28 (13.15%) had a normal level of smell according to three indicators; 22 patients (10.33%) have a zero level for all three indicators, that is, anosmia. In 185 cases (86.85%), the sense of smell was reduced in all studied indicators.

In a comparative analysis for each test separately in the main group of patients, a decrease in the sense of smell at the threshold was detected in 163 patients (76.53%): the assessment of olfactory disorders according to the threshold test varied from 0 to 9.5 points, the average score was  $2.6 \pm 1.4$  points. A decrease in the sense of smell according to the discrimination test was detected in 126 people (59.14%): the assessment of olfactory impairment varied from 0 to 16 points, the average score was  $8.7 \pm 4.2$ . A decrease in identification was detected in 169 people (79.35%): the assessment of olfactory impairment varied from 0 to 16 points, average values  $8.2 \pm 4.3$ . Of the 185 patients with a reduced sense of smell, 76 patients (41.08%) had anamnestic notes of these disorders even before the test (including 16 (8.65%) of them with anosmia). The majority of patients presented these complaints after a targeted survey, that is, dysfunction of the sense of smell was not among the daily complaints. We analyzed the relationship between subjective and objective assessment of the level of smell and the duration of the disease. With a duration of the disease <3 years, 104 (48.83%), with 59 (56.73%) men and 45 (43.27%) women, and the number who noted a decrease in sense of smell was 8 (7.69%) people, with PD duration up to 6 years - 51 (23.94%) patients, 29 (56.86%) men and 22 (43.14%) women, with PD duration up to 7 years - 31 (14.55%) patients, There were 18(58.06%) men and 13(41.94%) women, with PD duration up to 8 years - 27(12.68%) patients, 16(59.26%) men and 11(40.0%)

women. 74%). 18 (9.73%) patients noted a disturbance in their sense of smell before the onset of motor disturbances characteristic of PD.

Olfactory test results are better in women, i.e. There are gender differences. In women, the average OIE score was  $22.66 \pm 4.12$ ; in men, the average OIE score was  $16.58 \pm 2.78$ . According to the threshold, the average score for women is  $3.03 \pm 1.54$ , for men -  $1.86 \pm 2.18$ ; for discrimination, the average score for women is  $10.0 \pm 3.03$ , for men -  $7.58 \pm 2.60$ ; for identification, the average score for women is  $9.79 \pm 4.01$ , for men -  $7.14 \pm 5.16$ . Thus, according to all three tests, hyposmia is more pronounced in men.

**Conclusion.** The possibility of manifestation of hyposmia has been established; anosmia before the appearance of motor disorders is one of the important premotor signs in the diagnosis of early manifestations of PD. In Parkinson's disease, olfactory disorders are observed in 86.85% of cases, with violations of threshold (76.22%) and odor identification (79.46%) most often observed. Early parkinsonism in SA—hyposmia (87.09%) , anosmia (83.87%)—do not correlate with either the duration or the functional stage of the disease. Smell impairments in Parkinson's disease are statistically significant in men (total smell index  $16.6 \pm 2.8$  points) compared to women ( $22.7 \pm 4.1$ ).

Today, there is reason to believe that the presence of hyposmia in patients with early onset PD is an important biomarker of an underlying “parkinsonian” type neurodegenerative process and, consequently, the risk of future development of PD.

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