

## ORIGINAL ARTICLE

## Increased Frequency of Dermatological Diseases in Parkinson's Patients

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## ABSTRACT

**Objective:** To determine the frequency of seborrheic dermatitis, bullous pemphigoid, rosacea, and melanoma among the patients diagnosed with Parkinson Disease.

**Study Design:** Cross sectional study.

**Place and Duration of Study:** The study was carried out at Dermatology Department of Bakhtawar Amin Trust Teaching Hospital Multan from 13<sup>th</sup> May to 13<sup>th</sup> October 2020.

**Materials and Methods:** A total of 80 patients of Parkinson disease were evaluated for skin disorders. Disease severity was confirmed through Hoehn Yahr staging criteria (H-Y stage). Skin characteristics and disease diagnosis was made through finding sebum production levels, hot/cold flush test, immunofluorescence and biopsy evaluation for seborrheic dermatitis, rosacea, bullous pemphigoid, and melanoma, respectively. The test results were compared with control subject. Chi square test and student t-test were used to find the significance of results.  $P < 0.05$  will be statistically significant.

**Results:** Out of 80, 44 patients were positive for skin disorders. The frequency of seborrheic dermatitis was 31.2% and was quite high as compared to control group that was 25% whereas rosacea, bullous pemphigoid and melanoma was found in 15%, 6.2% and 2.5% patients and in control group they were 11.2%, 2.5% and 1.0% respectively. To detect the significant difference between quantitative variables of test and control group, chi square was used and student t-test was used to compare the qualitative variables.  $P < 0.05$  will be statistically significant.

**Conclusion:** Skin disorders are highly prevalent among Parkinson's patients than control population.

**Key Words:** Bullous Pemphigoid, Melanoma, Parkinson Disease, Skin Disorder, Seborrheic Dermatitis, Sosacea.

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## Introduction

Parkinson Disease (PD) is characterized as second most prevalent and progressive neurodegenerative disorder that was first elucidated by James Parkinson

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in his publication, 'Essay on the shaking palsy' in 1817.<sup>1</sup> The pathology develops mainly due to the loss of dopaminergic neurons in mid brain, substantia nigra, following the development of  $\alpha$ -synuclein aggregated cytoplasmic inclusions called as Lewy bodies. However, loss of non-dopaminergic neurons and involvement of other brain regions is also reported.<sup>2</sup> It has been estimated that every second person in 1000 is diagnosed of PD and the prevalence increases with age.<sup>3</sup> With the dramatic increase in global population, prevalence of PD is also likely to increase.

Clinically, PD manifests as triad of motor symptoms, including rigidity, tremors and akinesia.<sup>4</sup> However, in 98% of patients these motor dysfunction are usually preceded by non-motor abnormalities, including sleep disorders, bladder problems, constipation, depression, anxiety, apathy, excessive saliva, and

cutaneous problems.<sup>5,6</sup>

The latter has become topic of discussion since the advent of 20<sup>th</sup> century and research studies have validated the association of neurological disturbances in PD with cutaneous issues. Although the pathological cause behind the association is yet not fully understood, yet in certain cutaneous manifestations. Increased incidence of melanoma is related to increased levels of  $\alpha$ -synuclein in skin in PD. Few case reports attribute levo dopa therapy in PD as risk factor for melanoma.<sup>7,8</sup> Survey studies have found that dermatological problems in patients with PD significantly contributes to impair the quality of life. However despite of this, skin disorders usually go unattended by the treating physician.<sup>8</sup>

Therefore, it is mandatory to highlight the prevalence of skin disorders associated with PD to ensure the introduction of effective diagnostic and treatment strategies. Thus, the following study was conducted to determine the frequency of seborrheic dermatitis, bullous pemphigoid, rosacea, and melanoma among the patients diagnosed with PD.

### Materials and Methods

A cross sectional study was carried out at Dermatology Department of Bakhtawar Amin Trust Teaching Hospital Multan from 13<sup>th</sup> May to 13<sup>th</sup> October 2020. A total of 80 patients who were diagnosed with PD were randomly selected and classified for intensity of the disease according to Hoehn Yahr staging criteria (H-Y stage). The sample size was collected with a 5% probability error and 95% confidence level. Computer generated numbers were randomly allotted to the participants and were then categorized according to Hoehn Yahr staging system that describes progression of PD in five stages. The diseased subjects were compared with control group, who were positive for skin lesions but negative for PD, for the frequency of seborrheic dermatitis, bullous pemphigoid, rosacea, and melanoma to know either skin disorders linked with PD or not. Inclusion criteria includes patients of age 60 years or older with mild to moderate symptoms of PD. Patients with the history of any other neurological, dermatological or movement disorder were excluded from the study. Patients and controls were recruited in the study on first visit and the participants were asked to avoid bathing or use of cosmetics at least 6 hours before the examination for

the evaluation of skin disorders. Dermatological manifestations were observed on the second visit. Participants were investigated for medical history, demographics, medication and doses (if any). Left and right forehead, volar surface of forearm, and sternum was selected to measure the functions of skin during normal and humid temperature by using electrical probe-based instrument.<sup>9</sup> This instrument evaluates the water content present on upper most layer of the skin. To determine the fat content, sebumeter method was used.<sup>10</sup> Additionally, hydration and pH of the skin was measured using corneometer and pH electrode.<sup>11</sup> These function evaluation was critical to diagnose seborrheic dermatitis. A hot/ cold flush following spice intake was used to record clinical manifestation of rosacea. Detailed clinical examination of any apparent lesions of the skin were carried out and biopsy of any suggestive lesion was done for histopathological examination to diagnose melanoma or bullous pemphigoid. Bullous pemphigoid was confirmed by indirect immunofluorescence testing of serum.

### Data Analysis

SPSS 20.0 was used for analyses of the collected data. Frequencies were calculated for categorical variables like sex (Male and female) while age, Hoehn and Yahr, duration of PD were continuous variables and presented as mean with standard variation. Significance of the results were carried out using student's t-test and non-parametric Chisquare test.  $P < 0.05$  will be considered statistically significant.

### Results

A total of 80 patients with PD status were included in the study. Out of 80, 35 (43.7%) were women and 45 (56.2%) were male having average age of  $65.5 \pm 9.2$  years. Whereas, control group comprised of 80 individuals with no significant difference in distribution of age ( $64 \pm 9.8$ ) years and sex (Male: 47.5%, Female: 52.5%). Evaluation of clinical history revealed that majority of patients ranged between 2.0 to 3.0 stages according to Hoehn Yahr staging criteria while average mean duration of disease was found to be 8.3 years (Table 1).

Patients were on multiple medication therapy; however Levodopa, with variable dose, was taken by 70 (87.5%) of the patients (Table 2).

Evaluation of skin function test revealed that 31.2% of patients with PD suffering from seborrheic

**Table 1: Demographics of Patients with Parkinson Disease (n=80)**

Variables	Data
Sex	
Male	45(56.2%)
Female	35(43.7%)
Age, mean (SD)	65.5 (9.2)
Hoehn and Yahr, mean (SD)	2.4 (0.8)
Duration of PD, years	8.3 (6.2)

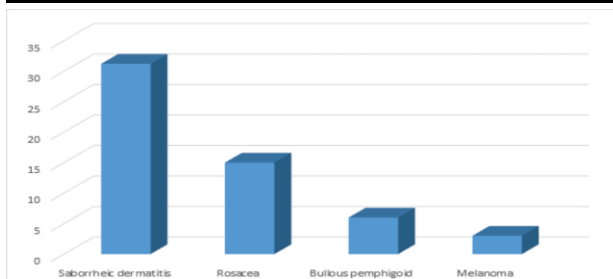
**Table 2: Frequency of Usage of Different Medication (n=80)**

Medications	Frequency (N %)
Levodopa	70 (87.5)
Tolcapone	5 (6.25)
Entacapone	15 (18.7)
Pramipexole dihydrochloride	25 (31.25)
Amantadine hydrochloride	18 (22.5)
Non-dopaminergic drugs	2 (3.7)

dermatitis. Right and left forehead (Total forehead) produced significantly high sebum ( $256.0\mu\text{g}/\text{cm}^3$ ) than in control subjects ( $184.0\mu\text{g}/\text{cm}^3$ ). Histopathological examination of biopsy diagnosed melanoma in 2.5% of patients. Among these 2.5%, majority (2.1%) had non-invasive melanoma. Rosacea and Bullous pemphigoid were diagnosed in 15% and 6% of patients. The incidences of these skin disorders were significantly high in PD patients than control (Table 3).

**Table 3: Characteristics of Skin Disorders among Patients with Parkinson Disease (n=80)**

Disease	Diseased Group	Control Group	P- Value
Seborrheic Dermatitis	25 (31.2%)	20 (25%)	< 0.05
Sebum Produce	$256.0\mu\text{g}/\text{cm}^3$	$184.0\mu\text{g}/\text{cm}^3$	< 0.05
Receiving L-Doper	340.15	318.2	0.55
Melanoma	2 (2.5%)	0.8 (1%)	0.001
Non-invasive Melanoma	2%	0.73%	-
Invasive Melanoma	0.5%	0.07%	-
Rosacea	12 (15%)	9 (11.2%)	<0.05
Bullous pemphigoid	5 (6.2%)	2 (2.5%)	<0.05



**Fig 1: Frequency of Skin Disorders Among Patients with Parkinson Disease (n=80)**

## Discussion

Parkinson disease is the growing concern around the world. However, motor symptoms are more widely under discussion than non-motor symptoms. The study focused on the cutaneous problems, non-motor symptoms, of PD. The basic aim behind the study was to determine the prevalence of four skin disorders among the patients diagnosed with idiopathic PD. It has been found that seborrheic dermatitis was the most prevalent disorder among the studied population. However, the prevalence rate of our study, 31.2%, is comparably low than the previous documented studies. A study conducted by Shahid et AL., noted seborrhoea dermatitis in 56.7% of patients.<sup>12</sup> Similarly, in another study 52-54% patients among studied population were diagnosed of seborrhoea dermatitis.<sup>13</sup> However, low prevalence rate in our study can be contributed to the effect of L-dopa.<sup>14</sup> A study by Gandhi RK suggested that L-dopa may slow the progression of Parkinson's disease and may have greater benefits even after stopping the drug.<sup>15</sup> Literature dictates that *Mallasezia* yeast contributes in the increased production of sebum and development of seborrhoea dermatitis.<sup>13</sup> Therefore, it can be interpreted that in PD conducive environment for yeast growth is created. However, how the neuronal changes associates with dermatological changes is yet to be fully explored. Rosacea was found to be second most prevalent disease in our study affecting 15% of studied population. These results are found to be in agreement with previous studies. According to a case-control study conducted on a Danish population, 7.62% of studied population was found to have coexistent PD and rosacea. It was concluded that increased metalloproteinase activity contributed to association between two disorders.<sup>16</sup> However, genetic predisposition is referred as major risk factor of rosacea development among PD patients.<sup>16</sup> Further, 6% of patients were diagnosed with bullous pemphigoid, a rate significantly higher than in control population that was 2.5%. The association of this cutaneous pathology with various neurological disorders is already well established. In a study conducted by Cordel et al., people with bullous pemphigoid having average age of  $83.8 \pm 7.5$  were evaluated and it was found that around 20% of such

people were having dementia.<sup>17</sup> Since bullous pemphigoid is an autoimmune disorders and both neurons and skin are derivatives of ectoderm, it is interpreted that autoantibodies directed against hemidesmosomal proteins in skin also target the same protein in neurons.<sup>18</sup> A study found that patients with already established bullous pemphigoid were at high risk of development of neurological symptoms and on-follow up it was observed that intensity of PD worsened with time.<sup>18</sup> Lastly, 2.5% of patients reported melanoma while in majority non-invasive form of tumour was reported. Although this low prevalence rate is consistent with previous studies.<sup>19</sup> In another study, the risk of development of melanoma was twice high in PD patients than normal individual.<sup>20</sup> Moreover, individuals with reduced darkness of hair colour were more likely to develop PD. Although, the exact mechanism behind this coexistence is hidden, but according a hypothesis  $\alpha$ -synuclein is responsible for the deposition of melanin in dopaminergic neurons.<sup>21</sup>

In our study although skin disorders are targeted and standard protocol is followed to get reliable results, but the study could be improved by disclosing the prevalence of other skin disorders. Moreover, effect of medications, especially L-dopa, is not thoroughly investigated. Patients should be evaluated by administering different dosage of dopaminergic and non-dopaminergic medications to determine their effect on cutaneous problems.

## Conclusion

Skin disorders is highly prevalent among Parkinson's disease patients than control population. The study invites further research in this area so that quality of life of patients could be improved.

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