Pakistan Journal of Intensive Care Medicine
eISSN: 2789-2905; pISSN: 2789-2891
www.pjicm.com
https://doi.org/10.54112/pjicm.v2022i1.11
Pak. J. Inten. Care Med., volume 2022: 11

Original Research Article

DERMATOLOGICAL ISSUES IN PATIENT WITH PARKINSON'S DISEASE

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Keywords
Skin disorder, Parkinson disease, seborrheic dermatitis, bullous pemphigoid, rosacea, melanoma

Received:
10th January 2022
Revised:
31th May 2022
Published:
Online 1rd June 2022

Abstract: *To determine the incidence rate of seborrheic dermatitis, bullous pemphigoid, rosacea, and melanoma among the patients diagnosed with Parkinson's Disease. A cross-sectional, observational study. From 13th May 2020 to 13th April 2022 at Bahria International Hospital, Lahore, Pakistan. A total of 80 patients with confirmed Parkinson's 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 the control subject. Chi2 and student t-test was used to find the significance of the results. Out of 80, 44 patients were positive for skin disorders. The incidence of seborrheic dermatitis was found in 31.2% of patients whereas rosacea, bullous pemphigoid, and melanoma were found in 15%, 6.2%, and 2.5% of patients, respectively. Skin disorders are highly prevalent among Parkinson's disease patients than in the control population. The study invites further research in this area so that the quality of life of patients could be improved.*

Introduction

Parkinson Disease (PD) is characterized as second most prevalent and progressive neurodegenerative disorder that was first elucidated by James Parkinson in his publication, 'Essay on the shaking palsy' in 1817 (Simon et al., 2020). The pathology develops mainly due to the loss of dopaminergic neurons in mid brain, substantia nigra, following the development of α-synuclein aggregated cytoplasmic inclusions called as Lewy bodies. However, loss of non-dopaminergic neurons and involvement of other brain regions is also reported (Sung and Nicholas, 2013). It has been estimated that every 2nd person in 1000 is diagnosed of PD and the prevalence increases with age (Tysnes and Storstein, 2017). 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 (Moustafa et al., 2016). 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 (Chaudhuri et al., 2006; Gros and Videnovic, 2020).

The latter has become topic of discussion since the advent of 20th century and research studies have validated the association of neurological disturbances in PD with cutaneous issues. Although the pathological causes behind the association is yet not fully understood, yet in certain cutaneous manifestations like melanoma involvement of α-synuclein and consequential effect of levodopa therapy is predicted (Gregory and Miller, 2015; Ravn et al., 2017). 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 (Ravn et al.,

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2017). 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 prevalence of seborrheic dermatitis, bullous pemphigoid, rosacea, and melanoma among the patients diagnosed with PD.

Methodology

A Cross sectional study, observational was conducted in Bahria International Hospital, Lahore for period of 23 months from 13th May 2020 to 13th April 2022. A total of 100 patients who were diagnosed with PD were included in study and classified for intensity of the disease according to Hoehn Yahr staging criteria (H-Y stage). The diseased subjects were compared with control, who were positive for skin lesions but negative for PD, for the incidence of seborrheic dermatitis, bullous pemphigoid, rosacea, and melanoma. Patients with the history of any other neurological, dermatological or movement disorder were excluded from the study. For the evaluation of skin disorders, the participants were asked to avoid bathing or use of cosmetics at least 6 hours before the examination. Left and right forehead, volar surface of forearm, and sternum was selected to measure the functions of skin during normal and humid temperature. To determine the fat content, sebumeter method was used (Qin et al., 2020). Additionally, hydration and pH of the skin was measured using corneometer and pH electrode (Algiert-Zielińska et al., 2018).These function evaluation was critical to diagnose seborrheic dermatitis. A hot/ cold flush following alcohol and 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 direct and indirect immunofluorescence testing of serum. Participants were also investigated for medical history, demographics and medication and their doses (if any).

Data Analysis

SPSS 20.0 was used for analyses of the collected data. Frequencies were calculated for categorical variables while continuous variables were presented as mean with standard variation. Significance of the results were carried out using student's t-test and non-parametric Chi^2 test.

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 ± 9.2 years. Whereas control group comprised of 60 individuals with no significant difference in distribution of age and sex. 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 I). Patients were on multiple medication therapy; however, Levodopa, with variable dose, was taken by 70 (87.5%) of the patients (Table II). Evaluation of skin function test revealed that 31.2% of patients with PD suffering from seborrheic dermatitis. Right and left forehead (Total forehead) produced significantly High sebum than in control subjects, in contrast to other examined sites. Histopathological examination of biopsy diagnosed melanoma in 3% of patients. Among these 3%, 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 III).

Table I: 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 II: 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)

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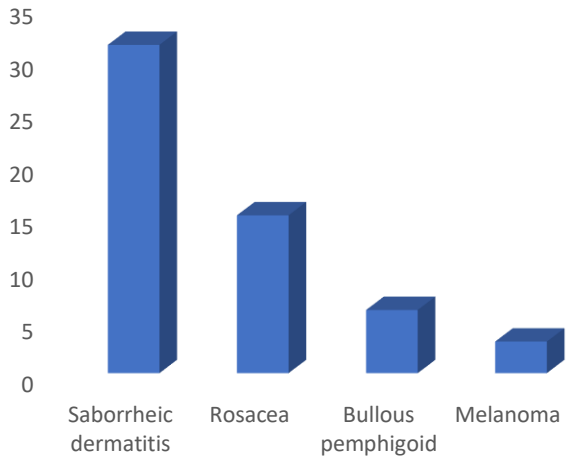
Table III: Characteristics of Skin Disorders among Patients with Parkinson Disease (n=80)

DISEASE	DATA	P-VALUE
Seborrheic Dermatitis	25 (31.2%)	< 0.05
Sebum Produce	256.0µg/cm^3(22)	< 0.05
Receiving L-Doper	340.15 (15.2)	0.55
Melanoma	2 (2.5%)	0.001
Margaret Melanoma	2.1%	-
Invasive Melanoma	0.4%	-
Rosacea	12 (15%)	<0.05
Bullous pemphigoid	5 (6.2%)	<0.05

Figure I: Prevalence 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. They 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 seborrhea 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 seborrhea dermatitis in 56.7% of patients (Shahid et al., 2020). Similarly, in another study 52-54% patients among studied population were diagnosed of seborrhea dermatitis (Arsenijevic et al., 2014). However, low prevalence rate in our study can be contributed to the effect of L-dopa (Adalsteinsson et al., 2020). Literature dictates that Mallasezia yeast contributes in the increased production of sebum and development of seborrhea dermatitis (Arsenijevic et al., 2014). Therefore, it can be interpreted that in PD conductive environment for yeast growth is created. However, how the neuronal changes associates with dermatological changes are 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 (Egeberg et al., 2016). However, genetic predisposition is referred as major risk factor of rosacea development among PD patients (Egeberg et al., 2016).

Further, 6% of patients were diagnosed with bullous pemphigoid. 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 were evaluated and it was found that around 20% of such people were having dementia, a rate significantly higher than in control population (Cordel et al., 2007). 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 (Brick et al., 2014). This interpretation is validated by many studies. 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 neurological presentation worsened with time (Brick et al., 2014). 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; yet significant association is reported between melanoma and PD (Liu et al., 2011). In another study, the risk of development of melanoma was twice high in PD

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patients than normal individual (Tanaka et al., 2018). 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 α-synuclein is responsible for the deposition of melanin in dopaminergic neurons (Pan et al., 2012).

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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