

Prevalence and Characteristics of Itch in Patients with Parkinson's Disease

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Patients with Parkinson's disease (PD) report increased pain sensitivity. Previous studies have found a larger area of itch hypersensitivity in PD patients, suggesting altered central processing. High levels of cutaneous α -synuclein, correlated with small-fibre neuropathy, may be another mechanism of pruritus in these patients. This study aims to characterize itch in PD patients without pruritic cutaneous disease and correlate it with disease characteristics. A total of 100 PD patients were surveyed using a modified numeric itch scale. Patients reporting chronic itch were included in the itch+ group. Demographic data were collected by retrospective chart review. In all, 41% of patients (41/100) reported itching. There was a significant correlation between PD duration and 24-h average itch severity (0.491, $p=0.002$). Itch is common among PD patients, with a positive correlation between PD duration and itch severity. Further research is needed to study larger cohorts and elucidate underlying pathomechanisms. Itch is often an underappreciated symptom of PD with potentially significant quality-of-life implications. This is among the first studies to characterize the prevalence and characteristics of itch in a substantial cohort of PD patients and how they may be related to other disease characteristics.

Key words: itch; Parkinson's disease; pruritus; prospective study.

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Parkinson's disease (PD) is a systemic illness, characterized by motor and non-motor symptoms. Non-motor manifestations are often under-appreciated but greatly impact quality of life. α -synuclein deposits, part of the pathology of Lewy bodies in PD, have been identified in the skin (1). Peripheral α -synuclein deposition has been hypothesized to contribute to prodromal PD symptoms (2) and to dermal nerve fibre loss and decreased epidermal nerve fibre density (3–5). The presence of α -synuclein has also been correlated with small-fibre neuropathy, suggesting a role in peripheral nerve damage (6). Additionally, prior work has found a

SIGNIFICANCE

Itch is a burdensome but frequently overlooked non-motor symptom in Parkinson's disease. Research in this field remains limited. This study demonstrates a high prevalence of itch in patients with Parkinson's disease, typically of moderate intensity and with neuropathic characteristics. These findings underline the clinical relevance of itch in this population, suggest possible underlying neuropathic mechanisms, and highlight the need for further research to improve recognition and management.

significantly larger area of itch hypersensitivity in PD patients following histamine application, suggesting a possible alteration in central processing (7).

PD is commonly associated with a range of itchy disorders including seborrheic dermatitis, bullous pemphigoid, rosacea, hypo- and hyperhidrosis, and medication side effects. As these skin pathologies may be levodopa-responsive, (2) further characterization of itch in PD patients is warranted.

Itch is a common symptom and is among the 50 most prevalent conditions worldwide (8, 9). A recent international study on the prevalence of itch by Yosipovitch et al. looked at over 50,000 individuals across 6 continents, representing a global population sample. The study found the worldwide prevalence of pruritus (acute and chronic itch) to be 39.8%, with a slight female predominance (40.7% vs 38.9% of women and men, respectively) (9). The estimated lifetime prevalence of chronic itch (>6 weeks) ranges between 8% and 25.5% (8, 10). One study showed that itch prevalence increased with age from 12.3% (16–30 years) to 20.3% (61–70 years) (11). The relationship between PD, itch prevalence, and associated characteristics is not well studied. The purpose of the current study was to determine the prevalence and characteristics of itch in patients with Parkinson's disease and whether there is a correlation with itch and disease characteristics.

METHODS

We surveyed 100 patients with PD, chosen at random from our movement disorders clinics at the University of Miami Miller School of Medicine, using a validated

numeric rating itch scale (**Fig. 1**) (12). Patients were included in the itch+ group if they reported chronic history of itch, defined as itch >6 weeks, on the questionnaire and did not have evidence of a pruritic cutaneous disease.

Retrospective chart review was performed to collect demographic data. Statistical analysis was then performed using the 2-tailed *t*-test for unpaired data to compare demographic data between groups. Pearson correlation

Itch Screening

Itch In The Past 24-HRS
 ▼

Total Itch Duration (e.g. 2 months)

24-HR Average Itch Severity
 ▼

24-HR Worst Itch Severity
 ▼

Itch Descriptors
☐ Burning ☐ Prickling ☐ Tingling ▼

Itch Distribution
☐ Localized ☐ Generalized ▼

Itch Location
☐ Scalp ☐ Chest ☐ Abdomen ☐ Back ☐ Buttocks ☐ Genitals ☐ Upper Extremity ☐ Lower Extremity ▼

Itch Orientation
☐ Symmetric ☐ Asymmetric ☐ Unilateral ☐ Flexor Surfaces ☐ Extensor Surfaces ▼

Scratch Pleasurability
 ▼

24-HR Total Itch Duration
 >9 hours"/> ▼

Itch Daily Pattern
☐ In the morning ☐ In the afternoon ☐ At night ☐ Intermittently ▼

Impact on sleep
 ▼

Aggravating Factors

Alleviating Factors

Itch response to treatment
 ▼

Fig. 1. Itch questionnaire.

Table I. Demographics of surveyed patients with Parkinson's disease

Factor	All	Non-itchy	Itchy	<i>p</i> -value
<i>n</i>	100	59	41	
Gender M/F	67/33	41/18	26/15	0.53
Age, years	68.11±10.95	67.93±11.31	68.37±10.53	0.85
Disease duration, years	7.88±5.66	7.95±5.03	7.78±6.53	0.88
UPDRS-III ON	22.34±10.52	20.68±10.54	24.61±10.18	0.07
UPDRS-III OFF	31.57±13.64	31.83±14.06	31.21±13.25	0.84
LEDD	566.92±412.57	589.31±385.85	534.71±451.22	0.53

UPDRS: Unified Parkinson Disease Rating Scale; LEDD: levodopa equivalent daily dose.

analysis was used to correlate itch characteristics with PD disease duration, Unified Parkinson's Disease Rating Scale (UPDRS) On/Off medication scores (defined by evaluation when patients' medications are working optimally vs when the effects are worn off, respectively), and levodopa equivalent daily dose (LEDD); $p < 0.05$ was considered significant. Statistical analysis was performed with the Statistical Package for Social Science Software (SPSS, version 29.0; IBM Corp, Armonk, NY, USA) for Windows. This study was approved by the IRB.

RESULTS

Of 100 PD patients surveyed, 41 reported itch. Full demographics are given in **Table I**. Average age, gender, PD disease duration, UPDRS-III On and Off scores, and LEDD were not statistically significant between groups. Males represented a higher proportion of the cohort, but this was not significantly different between groups with itch and no itch.

Among patients with itch, average itch duration was 6.16 ± 12.98 years and PD duration was 7.88 ± 5.66 years. Correlations were made between PD clinical characteristics and itch characteristics (**Table II**). There was a positive, moderate correlation between PD duration and 24-h average itch severity (0.491 , $p = 0.002$). When correcting for age, the correlation strengthened (0.522 , $p < 0.001$). The other correlations remained insignificant following correction for age.

On an 11-point Numerical Rating Scale (NRS), average 24-h itch severity and average 24-h worst itch were 4.63 ± 2.34 and 5.37 ± 2.61 , respectively. The most commonly reported 24-h itch duration was 0–2 h (94.74%), and scratch was rated as pleasurable with an average score of 3.06 ± 2.94 (scale; –5 to +5). The itch was most commonly characterized as having a burning quality

Table III. Itch characteristics in patients with Parkinson's disease

Itch characteristic	<i>n</i> (%)
Patients reporting itch	41/100
Total itch duration, years	6.16 ± 12.98
24-h average itch severity	4.63 ± 2.34
24-h worst itch severity	5.37 ± 2.61
24-h total itch duration	0–2 h: 36 (94.74%) 3–5 h: 1 (2.63%) > 9 h: 1 (2.63%)
Scratch pleasurability	3.06 ± 2.94
Descriptors	Burning: 11 (37.93%) Prickling: 6 (20.69%) Tingling: 3 (10.34%) Localized: 35 (87.50%) Generalized: 4 (10.00%) Mixed: 1 (2.50%)
Location	Scalp: 18 (43.90%) Back: 17 (41.46%) Upper extremity: 7 (17.07%) Lower extremity: 10 (24.39%)
Orientation	Symmetric: 20 (54.05%) Unilateral: 6 (16.22%) Extensor surfaces: 4 (10.81%) Flexor surfaces: 3 (8.11%)
Daily pattern	Intermittent: 31 (79.49%) Nightly: 8 (20.51%) Afternoon: 1 (2.56%)
Impact on sleep	No: 33/38 (86.84%) Yes: 5 (13.16%)
Aggravating factors	Dry skin: 4 (26.67%) Not bathing: 3 (20.00%) Hair products: 4 (26.67%) None identified: 4 (26.67%)

(37.93%), localized distribution (87.50%), on the scalp (43.90%) or back (41.46%), with a symmetric orientation (54.05%), an intermittent daily pattern (79.49%), and with no impact on sleep (86.84%) (**Table III**). Aggravating factors included dry skin, not bathing, and use of hair products.

DISCUSSION

This study was the first to examine itch and its characteristics in a meaningful cohort of PD patients. We report that localized itch is a common complaint in 41% of PD patients, which may suggest that this symptom is neuropathic in origin. The itch is related to disease duration but not necessarily to the motor severity of PD.

Non-motor manifestations of PD are under-recognized. Within that category, itch is very unlikely to be discussed, recognized, or treated. Often, itch is even ignored by the patient despite being significantly bothersome, as it is not generally thought to be related to PD. Recognition could

Table II. Correlations between Parkinson's disease clinical characteristics and itch

Item	Total itch duration, years			24-h average itch severity			24-h worst itch severity			Scratch pleasurability		
	<i>r</i>	<i>p</i> -value	<i>n</i>	<i>r</i>	<i>p</i> -value	<i>n</i>	<i>r</i>	<i>p</i> -value	<i>n</i>	<i>r</i>	<i>p</i> -value	<i>n</i>
Age	–0.055	0.761	33	–0.279	0.09	38	–0.332*	0.041	38	0.156	0.365	36
PD duration, years	–0.148	0.411	33	0.491*	0.002	38	0.252	0.127	38	0.171	0.319	36
UPDRS-III ON	0.089	0.622	33	–0.126	0.453	38	0.053	0.754	38	0.02	0.907	36
UPDRS-III OFF	0.118	0.557	27	–0.134	0.471	31	–0.137	0.464	31	0.07	0.719	29
LEDD (mg)	–0.109	0.545	33	0.12	0.473	38	–0.027	0.873	38	0.136	0.427	36

UPDRS: Unified Parkinson's Disease Rating Scale; LEDD: levodopa equivalent daily dose.

not only lead to a better understanding of the patient but also to symptomatic relief. Awareness of which patient demographics predispose a patient to different forms of itch, including differing severity and location, would allow us to be more precise in our management. In the future, this could serve as a platform to investigate itch as a biomarker for PD, as well as a harbinger for other cutaneous issues or impulse-control disorders.

Of note, the itch severity was rated as moderate and transient, and most patients did not report that it affected sleep. The authors therefore believe that aggressive therapies, such as with gabapentinoids, are unnecessary to treat itch of this severity, which differs from other common causes of neuropathic pruritus. Nevertheless, treatment may be warranted in some individuals if severity reaches a threshold such as to impact quality of life, and a more severe itch should prompt a dermatological evaluation to guide specific therapy if needed.

Among our patients with itch, the scalp and back were reported as the most common locations. These findings are consistent with the previously described skin biopsy findings of α -synuclein deposits in the scalp of PD patients (13) and the proximo-distal gradient of these deposits, with highest incidence in cervical regions followed by the back, then the extremities (6, 14). Given the growing use of α -synuclein skin biopsies, future correlations with biopsy findings among patients with itch may serve as a diagnostic biomarker. The mechanism of action may be related to small-fibre neuropathy secondary to α -synuclein deposits, systemic inflammation, and/or treatment side effects.

Other factors may be at play: central dysregulation may contribute to itch sensation as it has been demonstrated as a mechanism of central pain in PD, defined as tingling, burning, formication, or broadly, as neuropathic sensations, which may represent centrally mediated itch (15). Autonomic dysregulation and associated skin barrier disruptions may also contribute to itch. The relative pleasure of scratching in this cohort may represent a reactive neuroadaptive mechanism, whereby initial skin barrier defects initiate itch and the desire to scratch, which is further reinforced via a scratching-induced central reward mechanism involving residual dopamine release as suggested by preclinical studies (16,17). This may lead to further scratching and ultimately contribute to an itch-scratch cycle and neuronal sensitization. Furthermore, pruritus may occur secondary to primary pruritic dermatoses, several of which have been associated with PD, including seborrheic dermatitis.

Limitations

One limitation to our study is that patients self-reported their symptoms on the survey, raising the possibility of recall bias. This may partially explain why patients were not able to fill out all survey items, leading to

decreased power. Although patients did not undergo a formal dermatological exam, they had no frank clinical signs of primary dermatoses that could explain their itch. Nevertheless, confounders such as incipient seborrheic dermatitis in the scalp, which is rather rare, may have some minor impact. The back, the second most common itchy area, is not an area of seborrheic dermatitis or skin diseases associated with PD. Another potential limitation is in the potential concurrent polyneuropathy or small-fibre neuropathies of other aetiologies. In addition, although concurrent medications were looked at, the focus of our analysis was on levodopa equivalent dose.

Further research is indicated to better understand the associated pathophysiology of pruritus in PD, including an assessment of metabolic derangements such as correlations with vitamin B12 and B6 levels, which may be reduced in PD.

Conclusion

Our study is a step forward in understanding the interplay between pruritus, a highly prevalent comorbidity in the PD patient population, and how it relates to PD characteristics. Pruritus is an exceedingly common and sometimes debilitating sensation that may present as a primary disease or a symptom. The mechanisms and associations of itch are vast and widely varied. Its effects are underemphasized, but recently there has been a significant increase in research in the field. Studying pruritus in the context of common diseases such as PD provides us with a more comprehensive understanding of the disease and helps inform management to optimize our patients' quality of life. In this study, we found itch to be highly prevalent in PD patients and related to disease duration. We suspect that the pathophysiology may be related to small-fibre neuropathy, central dysregulation, autonomic alterations, and secondarily to associated primary dermatological conditions; nevertheless, further research on the underlying mechanisms of these associations is needed and will help improve PD patient outcomes.

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