Original Article

Pain Assessment in Indian Parkinson's Disease Patients Using King's Parkinson's Disease Pain Scale

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Abstract

Background: Pain is a common symptom in Parkinson's disease (PD) patients. Scales to rate pain in PD are marred by several flaws, either not being available in other languages or not specific for PD. **Objectives:** To assess the frequency of pain among bilingual Indian PD patients using "King's Parkinson's disease pain scale" (KPPS) and to validate it. **Methods:** We randomly administered KPPS in Hindi/English to all consecutive bilingual persons with PD. The results were appropriately analyzed. **Results:** A total of 119 PD patients were enrolled with a mean age of 64.34 (± 9.57) years. Median Hoehn and Yahr stage was 2 (42.85%). Pain was present in 62 (52.1%) PD patients. The most common type was musculoskeletal (74.19%). The mean total KPPS score was 16.02 ± 10.57. KPPS score was significantly higher in women and correlated positively with unified Parkinson's disease rating scale (UPDRS) part 2 and 4 scores (r = 0.27 and r = 0.25). Risk factors for pain were female gender, higher H and Y stage, total UPDRS score, and individual UPDRS part 3 and 4 scores. Difficulty falling asleep ($P = 0.01$), frequent awakenings ($P = 0.01$), diminished smell sensation ($P = 0.003$), diminished speech volume ($P = 0.02$), gait freezing ($P = 0.03$), and falls ($P = 0.001$) correlated with the presence of pain. The interclass correlation coefficient between the Hindi and English versions of KPPS was 0.835, while Bland–Altman analysis showed 96.7% agreement suggesting excellent correlation and validation. **Conclusions:** KPPS is an easy tool for characterization, scoring, and follow-up of pain in PD patients. The Hindi version has good agreement with the original English version.

Keywords: Hindi translation, KPPS scale, movement disorder, nonmotor symptoms, pain, PD

Introduction

According to recent estimates, about 6.3 million people worldwide suffer from Parkinson's disease (PD).[1] While diagnostic criterion emphasizes motor symptoms, nonmotor symptoms (NMS) are equally if not more debilitating to persons with PD. These NMS are sensory disturbance such as disturbance of smell, pain, and visual symptoms, fatigue, neuropsychiatric disturbances, autonomic dysfunction, and sleep disorders, and they adversely affect the quality of life (QoL) of these individuals.

Pain, an NMS, is one of the most common NMS, affecting up to 30% to 83% of PD patients.[2] It is frequently under-recognized and thus undertreated. Despite its high prevalence, it continues to be poorly treated and is also a key determinant of poor QoL. Pain in PD is usually noted on the side of the body that is either first or most affected by the disease, suggesting a relation to pathology in the basal ganglia.[3] Pain can also appear as a premotor feature and is therefore not recognized as a symptom of PD until motor manifestations appear. Some studies have indicated that pain symptoms in early and drug-naïve PD patients are associated with severity of motor disability.[4] The etiology/localization of pain is varied. It may vary from pain resulting due to generalized rigidity to restless leg syndrome.

Several correlates of pain in PD have been described such as depression,[5] motor fluctuations,[6] severity of PD,[7] female gender,[2] etc., Attempts to rate or assess pain in PD have been made by many authors.[8] These include unified Parkinson's disease rating scale (UPDRS), visual analog scale, brief pain inventory,[9] McGill pain questionnaire,[10] DoPaMiP study questionnaire (Douleur et maladie de Parkinson en Midi-Pyrénées),[8] Marburg-São Paulo-Créteil questionnaire,[11] Douleur Neuropathique questionnaire (DN-4),[12] Pain DETECT,[13] etc., However, these have not been validated specifically for PD patients, nor in other languages apart from which they were initially developed. Recently, Movement Disorders Society (MDS) has accepted pain scale devised under the stewardship of Chaudhuri *et al*.[14] named "King's Parkinson's Pain Scale," which has been tested by investigators other than the original developer on PD patients. It has adequate clinometric properties and has been validated in French and Spanish languages as well.

We aimed to estimate the occurrence of pain in PD patients at our out-patient clinic using King's Parkinson's Pain

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Scale (KPPS) in Hindi language spoken by most patients in India and to validate it.

Methods

The primary aim of the study was to assess the frequency of pain among bilingual (Hindi and English speaking) Indian persons with Parkinson's disease using Hindi and English (original) versions of KPPS and to validate it.

Secondary objectives of our study were to: evaluate frequency, severity, and types of pain in Indian Parkinson's patients using Hindi translation of KPPS and to test the association of pain in PD patients as assessed by KPPS with QoL, severity and stage of PD, gender, duration of PD, and presence of depression and anxiety.

The study was undertaken following International Conference on Harmonisation—Good Clinical Practice (ICH GCP) guidelines after obtaining Institution Review and Ethics Committee approval and participants' written informed consent.

For the study, we administered Hindi translation or original English version of KPPS to PD patients. The procedure of translation was followed as recommended.[15] The Hindi translation was done using simple Hindi words in general use. It was translated back in English by a bilingual neurologist who did not know about the scale. Two other neurologists looked at the Hindi translation and looked for any discrepancies in the meaning of the two versions (Hindi and English) of the scale and by mutual assent, corrections were made. The final version was sent to the original authors; they found some words which they thought were not appropriate as they thought they might go against the sensitivity of patients. Their suggestions were incorporated and sent back to them. After their approval, the final version was pretested on 8 PD patients. All found it easy to understand. Before going to patients for testing, it went through two rounds of discussion with the developers of the scale. The final version of Hindi translation was approved by the original developer of the scale. All the stakeholders, including 8 persons with PD, their caregivers, and neurologists involved in treating patients with PD ($n = 10$) looked at final translation and confirmed its correctness and confirmed that no stakeholder felt any embarrassment or difficulty while filling the form.

Subsequently all consecutive nondemented bilingual (Hindi and English speaking) persons with PD, fulfilling Queen Square PD Brain Bank Clinical Diagnostic criteria of PD[16] irrespective of age, gender, age of onset of symptoms, and duration of disease were recruited to participate after obtaining informed consent. Patients confirmed the presence of pain, as declared in item 10 of the NMS questionnaire (NMSQuest)[17] were included in the test group, whereas those without pain were included in the control group.

Inclusion criteria

a. All consecutive nondemented (MMSE score >/= 24) Indian bilingual PD patients satisfying the Queen Square PD Brain Bank criteria for the diagnosis of idiopathic PD[16] irrespective of age, gender, age of onset, duration of disease, severity of disease or drugs were included.

Exclusion criteria

a. Alternative or uncertain diagnosis of Parkinson's or drug-induced Parkinsonism.
b. Inability to give consent.
c. Dementia, as described above.
d. Diagnosis of disorders causing pain unrelated to PD (e.g., severe osteoarthritis/arthritis, malignancy, etc.

We administered KPPS in Hindi or English version in random order (English first or Hindi first) to all the consenting participants if they had pain anywhere in the body after determining the presence of pain on NMS scale (question no. 10).[17] The language to be tested on the first visit was chosen randomly using computer-generated random numbers. Clinical and demographic data were collected in the PD format, routinely used in the out patient's clinic. On the first visit, the following information was also collected: UPDRS (Parts 1, 2, 3 and total),[18] Hospital Anxiety and Depression Scale (HADS)—HADS-Anxiety score and HADS-Depression score, Parkinson's Disease Questionnaire-Short Form (PDQ8),[19] European Quality of Life Scale (EQ-5D),[20] and the Visual analogue scale for pain severity (VAS). After an interval of 10 ± 2 days, KPPS in the other language was administered (other than the language first used). All participants were asked to fill the pain scale alone or with the help of a caregiver. All the patients who had pain returned in 10+/−days. They were reminded on phone a few days in advance and an appointment was fixed. They all came within the time frame.

Data were entered and analyzed using Statistical package for Social Sciences version 24.0 (IBM, PASW Statistics, India Country office, Bangalore, India). The descriptive analysis including proportions, percentages, frequency distribution, and measures of central tendency was done. Chi-square and Fischer's exact test were applied to compare proportions and student's t-test was applied to compare means. KPPS score was correlated with demographic factors and other scores, and correlation coefficient was calculated. The agreement was tested by calculating the interclass coefficient (ICC) and by plotting the Bland–Altman plot.

Results

A total of 119 persons with PD were enrolled in the study from April 2016 to 1st April 2018. Demographic data are shown in Table 1. The mean age of the subjects at the time of enrolment was 64.34 (± 9.57) years (range: 32–80) years. The mean age of onset of symptoms was 56.59 (± 11.61) years, (range: 19–78 years). The most common Hoehn and Yahr stage was stage 2 seen in 42.85% cases ($n = 51$). Men formed 69.7% ($n = 83$) of the PD population. Table 1 shows the baseline clinical characteristics of the whole cohort. The mean duration of disease was 7.71 (± 5.55) years (range: 3

months–30 years) at the time of enrolment. Cognitive screening using MMSE showed the mean score of 26.65 ± 2.02 (range: 24–30). The mean total UPDRS score was 29.4 ± 22.45. Initial mean improvement with dopaminergic treatment was 63.28% (± 21.14, range: 15–100), while mean response to dopaminergic treatment at the time of enrolment was 54.79% (± 17.37, range: 10%–90%). Mean HADS-Anxiety score was 7.73 ± 3.17, while mean HADS-Depression score was 8.53 (range: 2–17). The mean quality of life assessments using PDQ8 and EDQ5D were 7.87 ± 4.03 (range: 0–18) and 3.92 ± 1.85 (range: 0–5), respectively.

Tremor was present in 63% participants (n = 75), whereas stiffness and slowness of activities of living were seen in 58.8% (n = 70) and 90.8% (n = 108) participants, respectively. Other NMS like diminished smell were seen in 18.5% (n = 22), low volume speech in 55.5% (n = 41), gait disturbances in the form of freezing in 37% (n = 44) individuals, and falls were seen in 35.3% (n = 42) of individuals. Sleep disturbances in the form of difficulty in falling asleep were seen in 24.4% (n = 29) of individuals; on the other hand, frequent awakenings from sleep was observed in 24.4% (n = 29), while restless leg syndrome was complained of by 12.6% (n = 15) participants [Table 2].

Sixty-two out of 119 (52.1%) PD patients reported some form of pain. The common types of pain observed in our cohort were [Table 3] musculoskeletal pain (pain around the joints) in 74.19% (n = 46) patients, radicular pain in 66.12% (n = 41), nocturnal pains in 59.67% (n = 37), chronic pain in 41.93% (n = 26), and fluctuation related pain in 41.93% (n = 26) in the form of pain during choreoathetotic (dyskinesia) movements in 11.29% (n = 7), pain due to off period dystonias in another 11.29% (n = 7), and generalized "off" period pain in 19.35% (n = 12). Other, less common pains were pain related to edema/swelling in 20.96% (n = 13) and the least common type of pain was orofacial pain which was seen in only 9 patients (14.28%).

Table 1: Baseline clinical characteristics of all study participants

Variables	*n*	Mean	Range
Mean age ±(years)	119	64.34±9.57	32-80
Mean age at onset ±SD (years)	119	56.59±11.61	19-78
Mean duration of PD±SD (years)	119	7.71±5.55	3 months-30 years
% men	119	Men (n=83) 69.74%	
UPDRS part 1	119	2.02±2.5	0-12
UPDRS part 2	119	10.39±7.75	0-39
UPDRS part 3	119	15.89±13.79	0-65
UPDRS part 4	119	1.14±2.55	0-17
UPDRS total	119	29.44±22.45	0-107
MMSE	117	26.65±2.02	24-30
Initial % response to dopaminergic meds.	119	63.28±21.14	15%-100%
Current % response to dopaminergic meds.	119	54.79±17.37	10%-90%
H and Y	119	2.27±0.92	1-5
HADS-Anxiety score	119	7.73±3.17	0-16
HADS-Depression score	119	8.53±3.16	2-17
PDQ8	92	7.87±4.03	0-18
EQ5D	92	3.92±1.85	0-5
KPPS Score	62	16.02±10.57	2-54

The mean total KPPS score of the whole cohort was 16.02 ± 10.57 (range: 2–54). The mean KPPS scores were significantly higher in women as compared to men (mean score: 20.13 ± 11.487 vs. 13.42 ± 9.173, P = 0.014) [Table 4] and had a weak correlation with severity of disease (UPDRS parts 2 and 4). KPPS scores correlated positively with UPDRS part 2 score (r = 0.27) and UPDRS part 4 score (r = 0.25) [Table 5]. ICC between the Hindi and English versions of KPPS was 0.835, while Bland–Altman analysis showed 96.7% agreement suggesting a very good correlation between the two languages [Figures 1 and 2].

Demographic and clinical characteristics of patients with and without pain showed no significant difference between mean ages (P = 0.58), MMSE scores (P = 0.94), duration of symptoms (P = 0.07), and age of onset of symptoms (P = 0.53) [Tables 2 and 6].

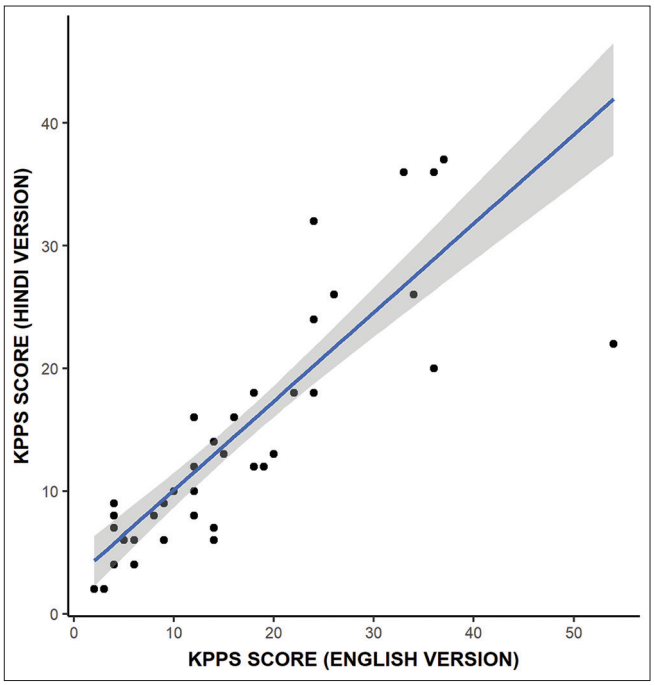

Figure 1: Scatterplot showing the correlation between KPPS Score (English Version) and KPPS Score (Hindi Version). Individual points represent individual cases. The blue trendline represents the general trend of correlation between the two variables. The shaded gray area represents the 95% confidence interval of this trendline. There was a strong correlation between KPPS Score (English Version) and KPPS Score (Hindi Version), and this correlation was statistically significant (Interclass Correlation Coefficient = 0.84, P = <0.001)

Table 2: Comparison of clinical characteristics of patients with and without pain

S. No.	Variables	PD patients with pain		PD patients without pain		Total		*P* (Chi-Square)
		n	%age	*n*	%age	*n*	%age	
1	Sex							
	Male	38	61.3%	45	78.9%	83	69.7%	**0.03**
	Female	24	38.7%	12	21.1%	36	30.3%	
2	Tremor							
	Yes	40	64.5%	35	61.4%	75	63.0%	0.72
	No	22	35.5%	22	38.6%	44	37.0%	
3	Stiffness							
	Yes	35	56.5%	35	61.4%	70	58.8%	0.58
	No	27	43.5%	22	38.6%	49	41.2%	
4	Slowness							
	Yes	57	91.9%	51	89.5%	108	90.8%	
	No	5	8.1%	6	10.5%	11	9.2%	0.64
5	Difficulty falling asleep							
	Yes	20	32.3%	9	15.8%	29	24.4%	**0.03**
	No	42	67.7%	48	84.2%	90	75.6%	
6	Frequent awakenings from sleep							
	Yes	21	33.9%	8	14.0%	29	24.4%	**0.01**
	No	41	66.1%	49	86.0%	90	75.6%	
7	Diminished Smell							
	Yes	17	27.4%	5	8.8%	22	18.5%	**0.009**
	No	45	72.6%	52	91.2%	97	81.5%	
8	Low Volume Speech							
	Yes	40	64.5%	26	45.6%	66	55.5%	**0.03**
	No	22	35.5%	31	54.4%	53	44.5%	
9	Freezing							
	Yes	29	46.8%	15	26.3%	44	37.0%	**0.02**
	No	33	53.2%	42	73.7%	75	63.0%	
10	Falls							
	Yes	31	50.0%	11	19.3%	42	35.3%	**0.001**
	No	31	50.0%	46	80.7%	77	64.7%	
11	RLS							
	Yes	11	17.7%	4	7.0%	15	12.6%	0.07
	No	51	82.3%	53	93.0%	104	87.4%	

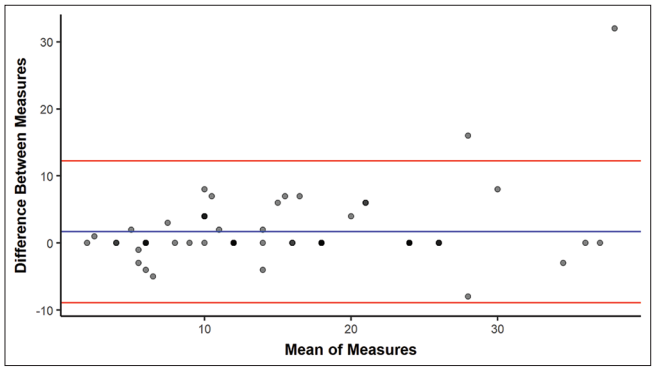

Figure 2: Bland–Altman plot comparing the mean of two measures (X-axis) to the difference between the two measures (Y-axis). The blue line represents the mean of the difference between the two measures, and the red lines represent the limits of agreement (mean ± 2SD of difference). Ideally, less than 5% of the observations should lie outside the limits of agreement. There was 96.7% agreement between the two measures, that is, 96.7% of the observations had a difference which was within the limits of agreement (±10.58)

Certain clinical features differed between PD patients with pain and those without pain. These were gender, H and Y stage, and UPDRS (parts 3, 4 and total scores). Women were in higher number in group with pain vs. those without pain (38.1% vs 21.1%, $P = 0.03$). The m ean H and Y stage was higher in patients with pain ($P = 0.02$); UPDRS (3, 4 and Total) scores were higher in patients with pain vs. those without ($P = 0.01$, 0.03, and 0.01, respectively). On the other hand, UPDRS parts 1 and 2 did not reach a statistically significant difference.

Among NMS, i.e., difficulty falling asleep ($P = 0.01$), frequent awakenings from sleep ($P = 0.01$), subjective diminished smell sensation ($P = 0.003$) and subjective diminished volume of speech volume ($P = 0.02$), freezing of gait ($P = 0.03$), and falls ($P = 0.001$) were significantly more common in PD patients with pain as compared to those without pain. Both initial response to levodopa and current response to levodopa were significantly lower in patients with pain ($P = 0.03$ and 0.04, respectively) as compared to those without pain.

Table 3: Types of pain in PD patients as measured by KPPS

S. No	Domain	*n*	Percentage	Mean	SD	Range
Domain 1: musculoskeletal pain						
1.	Pain around joints	46	74.19%	4.13	3.38	0-12
Domain 2: chronic pain						
2	Pain deep within the body	19	30.64%	1.56	2.60	0-8
3	Pain related to internal organ	7	11.29%	0.73	2.49	0-12
Domain 3: fluctuation-related pain						
4	Dyskinetic pain	7	11.29%	0.35	1.32	0-9
5	"Off" dystonia in a region 3	7	11.29%	0.44	1.51	0-9
6	Generalized "off" period pain	12	19.35%	1.05	2.61	0-12
Domain 4: nocturnal pain						
7	PLM or RLS-associated pain	15	24.19%	0.58	1.26	0-6
8	Pain while turning in bed	22	35.48%	1.98	3.35	0-12
Domain 5: Orofacial pain						
9	Pain when chewing	4	6.45%	0.13	0.59	0-4
10	Pain due to grinding teeth	2	3.22%	0.06	0.40	0-3
11	Burning mouth syndrome	3	4.83%	0.21	1.08	0-6
Domain 6: discoloration; edema/swelling						
12	Burning pain in the limbs	8	12.9%	0.68	2.15	0-12
13	Lower abdominal pain	5	8.06%	0.29	1.18	0-6
Domain 7: radicular pain						
14	Shooting pain/pins and needles	41	66.12%	3.82	3.49	0-12
15.	Total Score	62	100%	16.02	10.57	2-54

Table 4: Comparison of total KPPS score between men and women

SEX		*n*	Mean	Std. Deviation	*P* (*t*-test)
KPPS Total scores	Male	38	13.42	9.173	**0.014**
	Female	24	20.13	11.487	

Table 5: Correlation of KPPS scores with various factors

Variable	KPPS Total	
	r (Correlation coefficient)	*P*
Age	0.18	0.167
Duration of PD	0.09	0.467
Age of Onset of PD	0.10	0.440
UPDRS Part 1	0.05	0.698
UPDRS Part 2	0.27	**0.037**
UPDRS Part 3	0.16	0.228
UPDRS Part 4	0.25	**0.046**
UPDRS Total	0.21	0.08
H and Y Score	0.01	0.937
HADS-Anxiety score	0.20	0.114
HADS-Depression score	**0.25**	**0.051**
PDQ8	0.05	0.674
PDQ5	0.05	0.679
MMSE	-0.13	0.304

Discussion

The primary aims of the study were to assess frequency and types of pain among Indian Parkinson's disease patients using Hindi translation of KPPS and to validate the Hindi version in Indian PD patients.

In our cohort, more than half (52.1%) of persons with PD reported pain anywhere in the body. Although the mean age was 64.34 years, not different from many series, more of the patients had early-stage PD (H and Y stage 2 or less). Other authors have reported a much higher prevalence of pain in PD patients ranging from 70.3% to 88.6%.[21-23] Our results are similar to a review of the prevalence of pain among persons with PD, i.e., 59.7%.[24] Our study results are similar to a systematic review which cited the prevalence of pain 67.6%.[25]

Over-all the most common type of pain in our PD patients was musculoskeletal pain (74.19%) while orofacial pain was least common (14.28%) ($n = 9$). A similar pattern is reported by other authors as well.[20,22,23,26]

This is responsive to modification of dopaminergic dose and the result is very gratifying after identifying this pain and treating it.

The mean total KPPS score in our study was 16.02 ± 10.57, which was significantly higher in women. KPPS score in our cohort was similar to that in the cohort of 314 PD patients reported by Rodrıguez-Violante *et al*.[22] They also observed higher KPPS score in women as compared to men, a finding also reported by other authors.[27,28]

Risk factors of pain in PD are reported as female gender,[2] disease severity,[7] presence of depression,[29] sleep disturbances,[20] and motor fluctuations/dyskinesias.[30] We also observed pain significantly more commonly in women, (P-0.03). Additional

Table 6: Comparison of demographic and descriptive parameters between PD patients with pain and without pain

Variables	PD patients with pain ($n=62$)		PD patients without pain		*P* Students *t*-test
	mean	SD	Mean	SD	
Age	64.79	9.81	63.82	9.37	0.58
Duration of PD	8.57	6.17	6.74	4.63	0.07
Age at onset	55.97	11.98	57.29	11.24	0.53
UPDRS Part 1	2.11	2.17	1.91	2.85	0.66
UPDRS Part 2	11.43	6.94	9.21	8.49	0.12
UPDRS Part 3	18.75	14.42	12.68	12.41	**0.01**
UPDRS Part 4	1.62	3.15	0.61	1.47	**0.03**
Total UPDRS	33.68	22.49	24.84	21.67	**0.03**
%age efficacy of LD in early part of disease	59.44	18.97	67.46	22.70	**0.03**
%age efficacy of LD in current stage	51.69	15.71	58.16	18.58	**0.04**
H and Y	2.44	0.83	2.07	0.99	**0.02**
Anxiety	8.11	3.78	7.30	2.25	0.16
Depression	8.90	3.68	8.11	2.40	0.17
PDQ8	8.02	4.04	7.57	4.06	0.61
EDQ5	4.35	1.67	3.03	1.92	**0.01**
MMSE	25.44	3.78	25.50	4.27	0.94

factors associated with pain in our cohort of PD patients were disease severity (H and Y stage), UPDRS Score (parts 3, 4, and total), presence of freezing and falls, difficulty falling asleep, frequent awakenings from sleep, and diminished smell and speech volume.

Another observation in our study, not so far reported was that those PD patients who reported pain had a poorer initial response to dopaminergic therapy and continued to have poorer response even at the time of enrolment in the study. It may be possible that these patients have lower dopaminergic responsiveness and, hence, pain which is also due to low dopaminergic level does not respond to dopaminergic replacement. We at the moment are unable to explain the reason for this difference. We also believe that this fact may be due to other neurotransmitters operative in these patients such as endorphins or substance P, etc.

The Hindi and English version scores of the KPPS questionnaire showed excellent correlation (ICC of 0.835, while Bland–Altman analysis showed 96.7% agreement) providing a good validation for the Hindi translation of the KPPS scale.

To conclude, pain is a common and frequently underreported NMS of PD. Early identification and management is very gratifying and can significantly improve the QoL in PD patients. KPPS is an easy to use tool for characterization, scoring, and follow-up of pain in these people and as our study shows, Hindi version has a very good agreement with the original English version. This will allow this scale in Indian PD patients for wider use.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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