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Quality of life and caregivers' burden of Parkinson's disease

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Short title: Parkinson's disease patients and their care givers

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19

20 **Quality of life and caregivers' burden of Parkinson's disease**

21 **Abstract:**

22 **Aim**

23 This study focused on the impact of the clinical features on the QoL of PD patients, and of their
24 caregivers.

25 **Methods**

26 This study included PD patients along with their caregivers, and was undertaken at the
27 Malaysian Parkinson's Disease Association from June 2016 to November 2016. Clinical
28 features of PD patients were assessed using the Movement Disorder Society revised Unified
29 Parkinson Disease Rating Scale (MDS-UPDRS); the Hoehn and Yahr stage and the Schwab
30 and England Activities of Daily Living Scale were used to assess the severity and the ability
31 of Parkinson's disease patients respectively. QoL of PD patients was measured using the
32 Parkinson's Disease Questionnaire-39 (PDQ-39). The revised version of the Zarit Burden
33 Interview assessed caregiver burden.

34 **Results**

35 At least one of the clinical features affected PD patients' QoL, and at least one of the QoL
36 domains affected the caregivers' burden. Clinical features 'Saliva and Drooling', and
37 'Dyskinesia' explained 29% of variance in QoL of PD patients. The QoL domains 'stigma',
38 along with 'emotional wellbeing' explained 48.6% of variance in caregivers' burden.

39 **Conclusions**

The clinical features 'saliva and drooling' and 'dyskinesia' impacted the QoL of PD patients and the QoL domains 'stigma' and 'emotional wellbeing' of PD patients impacted their caregivers' burden.

Keywords: Carers; Malaysia; Quality of life; Clinical features; correlations.

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder with evolving layers of complexity [1]. Both motor and non-motor symptoms of PD may affect patients' quality of life (QoL) [2, 3]. Recent developments in the diagnosis and advanced management of PD have increased the patients' life expectancy towards that to the healthy individuals [4]. Therefore, improvement of the QoL is a significant part of therapeutic plans.

Patients with PD, especially those who are in advanced stages, are in great need of assistance, mostly from their family members or caregivers in terms of medical, emotional, and social support [5]. The role of a caregiver becomes increasingly important with the progression of PD, the severity of motor impairment and increasing age of the patient. The nature and symptoms associated with PD can place significant stresses on the caregivers' burden. As the prevalence of PD is estimated to more than double by 2030 [6], it is important to recognize and alleviate the burden experienced by caregivers [7].

Many studies conducted on QoL of PD patients were based on the effects of 'non-motor aspects' and 'motor aspects' [1-3]. Few studies have reported the 'motor examination' and 'complications' that affect the QoL in PD patients. However, no study has yet been undertaken to include all these aspects (clinical features) together to determine their influence on QoL of PD patients. Similarly, there are no studies on the aspect of PD patients' QoL which impact on their caregivers' burden.

In the present study, we examined the impact of clinical features (motor aspect, non-motor aspect, 'motor examination' and 'complications') on PD patients' QoL, and the impact of PD patients' QoL on their caregivers' burden.

Methods

Study Population and duration

We conducted this study at the Malaysian Parkinson's Disease Association from June 2016 to November 2016. The study included PD patients who have caregivers. Both the patients and caregivers were required to be aged 18 years or above. PD patients who did not have caregivers, and those who were not interested in this study were excluded.

Study design and study participants

This cross-sectional study was done using a convenience sampling method. Each participant gave written, informed consent in accordance with the ethical approval of Joint Committee for Ethics and Research (BP I-1-13 (13) 2016). All the participants were informed about the anonymity and confidentiality of the recorded responses. Out of 153 PD patients invited, 135 PD patients participated in this study along with their caregivers. Sample size was calculated using Raosoft software, a required sample size of 110 was demonstrated; power 80%, distribution of response 50%, with 95%confidence interval and 5% margin of error.

Clinical features assessment of PD patients

Clinical features of PD patients were assessed using the scale the Movement Disorder Society revised Unified Parkinson Disease Rating Scale (MDS-UPDRS) [8]; Hoehn and Yahr stage [9] and Schwab and England Activities of Daily Living Scale [10] were used to assess the severity and the ability of Parkinson's disease patients respectively. A prior permission from the

Movement Disorder Society was a prerequisite and it was obtained through email communication.

Parkinson's disease Questionnaire (PDQ-39) to measure quality of life

QoL of PD patients was measured using the Parkinson's Disease Questionnaire-39 (PDQ-39), which consists of 39 items within the following eight domains: *mobility, activities of daily living, emotional well-being, stigma, social support, cognition, communication, and bodily discomfort.* The scores on the PDQ-39 range from 0 (never have difficulty) to 100 (always have difficulty), with higher scores reflecting poorer QoL [11]. The domain score = sum of scores of each item in the domain divided by the maximum possible score of all the items in the domain, multiplied by 100. Lower scores reflect better QoL.

Zarit Burden Interview scale (ZBI) to measure caregivers' burden

The revised version of the Zarit Burden Interview [12 was used to assess caregiver burden. All 22 items on the ZBI are rated on a 5-point scale from 0 (*not at all*) to 4 (*extremely*), and a higher ZBI score indicates a higher level of caregiver burden.

Reliability Validity and of the questionnaire

All the questionnaire underwent internal consistency (reliability) and content validity prior to its administration to a small group of 10 samples for a pilot study. For the final analysis, the data of the pilot study were not used.

Data collection procedure

In Malaysian Parkinson's Disease Association, people with Parkinson along with their care givers meet every week. During this period, our researchers approached the people with Parkinson individually in a separate room. Standard questionnaires were used to evaluate the clinical features and quality of life of the people with Parkinson. Self-administered caregiver

burden scale was used on the care givers of separately. All the respondents were evaluated by a research professional who is specialised in Parkinson's disease using UPDRS scale, Modified Hoehn and Yahr Scale and Schwab and England activities of daily living scale. PDQ-39 scale was filled by the respondents. The questionnaire administrated was in English. However, those who had difficulty to fill and understand due to any clinical issue and/or language barrier, the questionnaire were helped by the researchers by getting the response from respondents.

Statistical Analysis

The Statistical Package for Social Science (SPSS) software "version 21" was used for data analysis. Demographic details of the patients and care givers were presented in frequency, percentages and mean with standard deviation. Nonparametric tests was used as the data did not meet the normal distribution as the data collected was convenience sampling method. The UPDRS, PDQ-39 and ZBI scales were calculated according to the standard scoring algorithms. The Mann-Whitney test was used to determine the significance of differences in QoL (PDQ-39 summary index scores) between PD patients who have certain clinical features and those who have not, as determined by UPDRS scores. Spearman rank correlation coefficients were calculated to assess the direction and magnitude of correlation between the clinical features of the PD patients and the QoL. Similarly, the Mann-Whitney test was used to determine the significance of differences in caregivers' burden (ZBI scores) between PD patients' QoL domains which were poor and those domains which were not, as determined by PDQ-39 domains scores. Spearman rank correlation coefficients were calculated to assess the direction and magnitude of correlation between the PDQ-39 domains and the caregivers' burden. Stepwise multiple logistic regression analysis was undertaken to determine the factors that best accounted for variance in QoL and caregivers' burden. Statistical significance was accepted at $p<0.05$.

Results

122 out of 135 PD patients responded completely to the questionnaire, giving a 90% response rate. There were no incomplete data. Baseline characteristics of the study population are shown in Table 1.The respondents' mean age was 58.1 ± 5.2 years, 56.5% of them were men, and the mean disease duration was 10.6 ± 8.4 years. The overall mean scores for the UPDRS scale indicates that, on average, the respondents' clinical features were from mild to moderate range. Based on the Hoehn and Yahr Scale, about 60% (n=74) of the respondents were in stage 2 (bilateral involvement without impairment of balance) and stage 2.5 (mild bilateral disease with recovery on pull test).

Schwab and England activities of daily living scale rating showed that 61% (n=75) of the respondents were "not completely independent" and 20% (n=25) of the respondents showed "some dependency" (Table 1).

130 caregivers responded completely to the questionnaire out of 135 caregivers (96% response rate). There were no incomplete data. All caregivers were close relatives of the respondents, and most were providing full-time care, with a mean duration of caregiving of 7.2 years. About 70% (n=88) of the care givers experienced moderate to severe burden. The characteristics of the caregivers are given in table 2.

Respondents with clinical features (non-motor aspects) such as 'hallucinations and psychosis', 'depressed mood', and 'urinary problems' had significantly different PDQ-39 summary index scores compared to the respondents who did not have these features (Table 3). However, other clinical features (non-motor aspects) such as; 'features of dopamine dysregulation syndrome' 'anxious mood', 'cognitive impairment', 'sleep problems', 'apathy', 'constipation problems', 'fatigue', 'daytime sleepiness', 'pain and other sensations' and 'light headedness on standing'

did not show any significant difference in QoL (PDQ-39 summary index scores), although some of the respondents had these clinical features.

In the same way, respondents with clinical features (motor aspects) such as 'saliva and drooling', 'walking and balance', 'dressing' and 'getting out of bed/ car/ a deep chair' had significantly different PDQ-39 summary index scores compared to the respondents who did not have these features (Table 3). However, other clinical features (motor aspects) such as 'eating tasks', 'speech', 'tremor', 'hygiene', 'chewing and swallowing', 'doing hobbies', 'turning in bed', 'freezing' and 'handwriting' did not show any significant difference in QoL (PDQ-39 summary index scores), although some of the respondents had these clinical features. Among the motor examination and complications, 'gait' and 'dyskinesia' had significantly different PDQ-39 summary index scores (Table 3). Also, there was no difference in PDQ-39 summary index scores with respect to respondents' age, gender and duration of disease.

Respondents' PDQ-39 domains scores for 'activities of daily living', 'mobility', 'emotional wellbeing', and 'stigma' showed significant difference in caregivers' ZBI scores (Table 4). However, other PDQ-39 domains scores such as 'communication and bodily discomfort', 'cognition', and 'social support' did not show significant differences in caregivers' ZBI scores. Also, there was no significant difference in caregivers' burden scores with respect to caregivers' age, gender and years dedicated as caregiver, and the number of days providing care in a week.

All the clinical features that showed significant difference in the QoL, overall UPDRS scores, PDQ-39 scores and ZBI scores were included in the Spearman correlation analysis (Table 5). The UPDRS scores were significantly and positively correlated with the PDQ-39 scores ($r = 0.68$, $p = 0.004$). This indicates, unsurprisingly, that as the clinical features of disability increase the QoL of the respondents becomes worsen. The clinical feature of 'hallucinations

and psychosis' positively correlated with the PDQ-39 domains 'stigma' ($r = 0.62$, $p = 0.02$) and 'emotional wellbeing' ($r = 0.52$, $p = 0.04$). The clinical feature 'saliva and drooling' was also significantly and positively correlated with PDQ-39 domains 'stigma' ($r = 0.60$, $p = 0.03$) and 'emotional wellbeing' ($r = 0.58$, $p = 0.04$). The clinical feature 'gait' was significantly and positively correlated with another clinical feature 'dyskinesia' ($r = 0.41$, $p = 0.05$); this indicates multicollinearity. The clinical feature 'dyskinesia' was significantly and positively correlated with PDQ-39 domains 'stigma' ($r = 0.52$, $p = 0.04$) and 'emotional wellbeing' ($r = 0.50$, $p = 0.05$). Other clinical features such as; 'depressed mood', 'urinary problems', 'walking and balance', 'dressing', 'getting out of bed, a car, or a deep chair' did not show any correlations.

There was a significant positive correlation between the PDQ-39 scores and the ZBI score ($r = 0.76$, $p = 0.003$). This indicates that, as the QoL of respondents gets worsen the caregivers' burden also get worsen. There was a significant positive correlation between the PDQ-39 domain 'stigma' and the 'ZBI score' ($r = 0.63$, $p = 0.01$). Also, there was a significant positive correlation between the PDQ-39 domain 'emotional wellbeing' and the 'ZBI score' ($r = 0.58$, $p = 0.03$). Other PDQ-39 domains such as; 'mobility' and 'activities of daily living' did not show any correlations.

To determine which clinical features contributed to impair the QoL, stepwise linear regression was performed by including all factors that had correlations with QoL scores (Table 5).

Before conducting multiple regressions, the correlations among the predictor variables should be checked. Since there was a correlation between clinical features 'gait', and 'dyskinesia' ($r = 0.41$, $p = 0.05$), multicollinearity was considered. Hence a separate linear regression analysis was performed for 'gait' and 'dyskinesia' against PDQ-39 summary index score. As a result, the 'gait' F value was too low and p value was not significant ($F(1, 135) = 15.81$, $R^2 = 0.137$, $p = 0.41$) whereas for 'dyskinesia', the F value $(1, 135) = 35.26$, with a $R^2 = 0.437$, and $p =$

0.03. Since the p value was significant, 'dyskinesia' was included in the multiple regression and 'gait' was excluded.

After running the multiple regression analysis, the best model was taken into account. Thus, model 2, with the clinical features such as 'saliva and drooling', and 'dyskinesia' explained 29% of variance in QoL scores ($F(3, 135) = 55.48$, $R^2 = 0.292$, $p=0.005$). The non-significant contributor 'hallucinations and psychosis' was excluded automatically by the SPSS software.

To determine which PDQ-39 domains contributed to the burden of caregivers, stepwise linear regression was performed by including all factors that were shown to have a correlation (Table 5). Only two factors (stigma and emotional wellbeing) significantly affected the caregivers' burden. In model 1, the 'stigma' variable explained 42.2% of the caregivers' increased burden ($F(1, 130) = 75.92$, $R^2 = 0.422$, $p= 0.005$). In model 2, 'stigma' along with 'emotional wellbeing' were the significant predictors with $F(2,130) = 80.43$, $R^2 = 0.486$, $p = 0.001$ (48.6% explained variance). Since the model 2 R^2 value was higher than that of model 1, model 2 was selected in this study, with model 2 showing an additional 6.4% of variance explained by the 'emotional wellbeing' variable in relation to the caregivers' burden.

Discussion

As this study had a high response rate, the results may be generalised to a wider population of people with PD and caregivers. Our study revealed that at least one of the clinical features in 'non-motor aspects', 'motor aspects', 'motor examination' and 'complications' has impacted the QoL of PD patients. The non-motor aspects such as 'hallucinations and psychosis', 'depressed mood', and 'urinary problems' had also significantly affected the QoL. Chronic exposure to dopaminergic medication is one of the main causes of hallucinations and psychosis [13]. Depression in PD is multifactorial, with possible contributions from dysfunctions in dopaminergic, serotonergic and noradrenergic systems [14]. Urinary dysfunction, which is a

manifestation of autonomic failure, is common in PD patients and significantly impacts on an individual's QoL [15].

Concerning motor aspects, 'saliva and drooling', 'walking and balance', 'dressing' and 'getting out of bed/car/a deep chair' significantly affected the QoL. Drooling causes psychosocial consequences and affects patient's QoL [16]. The loss of dopaminergic neurons from the substantia nigra pars compacta affects the walking ability and balance [17]. PD patients perceive that they need help from others at some time to even to manage their daily living activities; this contributes to the loss of independence [18]. Gait abnormalities and dyskinesia in PD patients may occur due to dopamine drug on-off fluctuations and this has a direct effect on their QoL [19, 20].

The PDQ-39 QoL domains such as 'mobility', 'activities of daily living', 'emotional wellbeing' and 'stigma' impacted on the caregivers' burden and this is supported by other published literature. Mobility impairment, as well as activities of daily living, have been reported as a burden for caregivers [21]. Increasing disabilities in PD construct a stigma that can lead to social isolation and emotional distress, which, in turn, causes burden to caregivers [22].

Our results revealed that the clinical feature 'hallucinations and psychosis' significantly correlated with the QoL domains 'stigma' and 'emotional wellbeing'. These two QoL domains directly reflect the society, family members and environment where they live. PD patients with hallucinations and psychosis are stigmatised and emotionally affected, and they choose not to tell anyone about these, because they are afraid of being perceived as cognitively incompetent. [22, 23]. The clinical feature 'saliva and drooling' significantly correlated with the QoL domains 'stigma' and 'emotional wellbeing'. 'Saliva and drooling' constitutes one of the most bothersome and troubling problems, often causing stigmatisation and affecting emotional

wellbeing of the people with PD, leading to social embarrassment and isolation [24]. Another clinical feature 'dyskinesia' significantly correlated with the QoL domains 'stigma' and 'emotional wellbeing'. Dyskinesia decreases the QoL in PD patients by affecting their emotional health because of stigmatisation [25].

PDQ-39 QoL domains 'stigma' and 'emotional wellbeing' were significantly correlated with the caregivers' burden. Stigma experienced by the PD patients affects their caregivers. Stigma and emotional wellbeing may lead to social elimination [22].

Multiple regression analysis revealed that clinical features 'saliva and drooling', and 'dyskinesia' are the significant contributors that impact on the QoL of PD patients. Psychosocially, drooling in PD patients in one of the primary reasons for poor QoL, emotional distress and social embarrassment [26]. Besides this, PD patients with drooling problems increased their caregivers' burden [27]. This clearly indicates that 'sialorrhoea' in PD patients affects their QoL which in turn reflects on their care givers' burden. On the other hand, the impact of dyskinesia as a key factor on QoL in PD patients has not been fully elucidated. Sitek (2011) explained the relationship between dyskinesia and 'stigmatization' which may impact the QoL of PD patients [28]. 'Stigma' and 'emotional wellbeing' are the significant contributors that impact the caregivers' burden. Stigma is a unique contributor that impacts on caregivers' burden. [29, 30].

Limitations

The QoL in PD patients may also be altered by many factors other than clinical features which are not captured in this study. Though the caregivers' burden was measured, the QoL of caregivers was not studied.

Conclusions

The QoL in PD patients is determined by at least one of the clinical features in 'non-motor aspects', 'motor aspects' 'motor examination' and 'complications'. The clinical features 'saliva and drooling' and 'dyskinesia' have significantly impacted the QoL of PD patients. The caregivers' burden is determined by at least one of the QoL domains. The QoL domains 'stigma' and 'emotional wellbeing' significantly impacted the caregivers' burden.

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Disclosure: All authors have approved the final article.

Authorship

1. the conception and design of the study, or acquisition of data, or analysis and interpretation of data: KIR, SJY
2. drafting the article or revising it critically for important intellectual content: KIR, MMK, SL
3. final approval of the version to be submitted: KIR, MMK

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386

387 **Table: 1 Patients' characteristics (n=122)**

Parameters	n	%
Hoehn and Yahr stage:		
1	7	5.7
1.5	16	13.1
2	38	31.1
2.5	36	29.5
3	19	15.5
4	4	3.2
5	2	1.6
Schwab and England activities of daily living scale		
80%- Completely independent, Conscious of difficulty and slowness	22	18.8
70% -Not completely independent	75	60.8
60% -Some dependency	25	20.4
Medications		
Levodopa	22	18
Levodopa + other Parkinson drugs	96	78.6
No drugs for Parkinson	4	32.4
Gender ratio		
Male: Female	69:53	56.5:43.5
	Mean	**SD**
Age in years	58.1	5.2
Disease duration in years	10.6	8.4
UPDRS score	72.8	30.2

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389

390 **Table: 2 Care givers' characteristics (n=130)**

Parameters	n	%
Gender ratio		
Male: Female	43:87	29.2:69.8
Little or no burden	17	13.1
Mild burden	25	19.2
Moderate burden	56	43.1
Severe burden	32	24.6
	Mean	**SD**
Age in years	45.1	10.2
Years dedicated as caregiver	7.2	6.4
Number of days providing care in a week	6.2	1.2

391

392 **Table: 3 Clinical features that significantly affected the quality of life scores**

Clinical features experienced by the participants	Mean of PDQ-39 summary index scores (SD)	p value
Non-Motor Aspects of Experiences of Daily Living		
Hallucinations and psychosis	45 (19.2)	0.005
Depressed mood	39 (18.6)	0.04
Urinary problems	33 (17.4)	0.02
Motor Aspects of Experiences of Daily Living		
Saliva and Drooling	43 (16.8)	0.003
Walking And Balance	36 (15.9)	0.05
Dressing	34 (18.2)	0.04
Getting out of bed, a car, or a deep chair	41 (17.1)	0.04
Motor Examination		
Gait	39 (19.3)	0.02
Motor Complications		
Dyskinesia	39 (19.4)	0.04

393 p value>0.05

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Table: 4 PDQ-39 domains scores significantly affected caregivers' burden scores

Mean PDQ-39 domains scores (SD)	Mean of ZBI scores (SD)	p value
Mobility- 32 (15.4)	55 (19.2)	0.05
Activities of daily living- 19 (8.1)	39 (18.6)	0.04
Emotional wellbeing- 22 (10.3)	61 (17.4)	0.002
Stigma- 15 (7.5)	66 (16.8)	0.003

p value>0.05

402 **Table 5: Quality of life correlates with clinical features and care givers' burden**

	Hallucinations and psychosis	Saliva and Drooling	Gait	Dyskinesia	Stigma				ZBI score
hallucinations and psychosis	1								
Saliva and Drooling	0.28	1							
Gait	0.54	0.45	1						
Dyskinesia	0.42	0.44	0.41*	1					
Stigma	0.62*	0.60*	0.48	0.52*	1				
Emotional wellbeing	0.52*	0.58*	0.35	0.50*	0.40	1			
UPDRS score	0.40	0.42	0.40	0.37	0.31	0.33	1		
PDQ-39 score	0.38	0.45	0.28	0.30	0.34	0.36	0.68**	1	
ZBI score	0.43	0.44	0.37	0.35	0.63*	0.58*	0.41	0.76**	1

403 * p <0.05, ** p<.005

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