Jurnal Kesehatan Prima

http://jkp.poltekkes-mataram.ac.id/index.php/home/index

p-ISSN: 1978-1334 (Print); e-ISSN: 2460-8661 **(***Online*

Parkinson’s Disease Quality of Life: Disease Severity Outweighs Pain Impact

Neila Raisa [1]✉, Yulianda Maziya[2], Annisa Rahma[3], Novita Titis Harbiyanti[4], Shahdevi Nandar Kurniawan[5]

[1-5] Universitas Brawijaya, Indonesia

✉ neilaraisa@ub.ac.id, Phone: +6281803805813

Received: 22 March 2024 /Accepted:18 August /Published Online: 31 August 2024

© This Journal is an open-access under the CC-BY-SA License

Abstract

Parkinson's disease is the second most common neurodegenerative disorder after Alzheimer's disease, progressively affecting both motor and non-motor systems in patients. In addition to the commonly recognized motor symptoms such as tremor, rigidity, and bradykinesia, non-motor symptoms such as chronic pain are often underdiagnosed. Pain in Parkinson's patients can manifest in various forms, including musculoskeletal pain, neuropathic pain, and dystonic pain. While pain is not a primary symptom defining Parkinson's, its impact on patients' quality of life is profound, contributing to reduced mobility, sleep disturbances, increased risk of falls, and poor mental health, including depression and anxiety. This study aimed to explore the relationship between the severity of Parkinson's disease, pain levels, and quality of life in Parkinson's patients. A cross-sectional observational study was conducted at the Neurology Clinic of RSUD Dr. Saiful Anwar in East Java from October 2023 to March 2024, using purposive sampling techniques. We assessed Parkinson's severity (Hoehn & Yahr scale), pain levels (Numeric Rating Scale), and quality of life (Parkinson's Disease Questionnaire-39 (PDQ-39) Indonesian Version).The study found that PDQ-39 INA scores were significantly associated with Parkinson's disease severity ($n = 11$, $p = 0.012$), indicating a significant impact of disease severity on quality of life. However, no significant relationship was found between PDQ-39 scores and pain levels ($p = 0.117$). Pearson correlation analysis showed no significant relationship between Parkinson's severity scale and pain level ($r = 0.461$, $p = 0.154$). Specifically, Parkinson's severity significantly affected PDQ-39 scores ($p = 0.001$), while pain levels did not have a significant effect ($p = 0.399$). This study reveals that while pain is a critical issue, it is the severity of Parkinson's disease that has a more substantial impact on patients' quality of life.

Keywords: Parkinson's Disease Severity; Pain Levels; Quality of Life; Parkinson's Disease

INTRODUCTION

Parkinson's disease is a common neurodegenerative disorder among the elderly, with a higher incidence observed in men. This condition affects approximately 1.5% to 2.0% of individuals over the age of 60 and 4% of those over 80 years old (Marino et al., 2020). The etiology of Parkinson's disease involves a complex interplay of genetic, epigenetic, and environmental factors (Andrew et al., 2021). Clinical manifestations typically emerge after 70-80% of dopaminergic neurons have been damaged (Emamzadeh & Surguchov, 2018).

Chronic pain is a significant health concern that adversely affects patients' lives, causing functional, social, economic, and emotional changes that disrupt their quality of life (Pereira et al., 2021). Pain is a common symptom among Parkinson's patients, occurring two to three times more frequently than in age-matched individuals without the disease. Pain may precede motor symptoms by several years and is a dominant non-motor symptom in patients with a disease duration of less than six years, particularly when originating from musculoskeletal or visceral sources. Despite its high prevalence, approximately 40% of patients may not report pain during routine clinical consultations (Young Blood et al., 2016).

Pain in Parkinson's disease is also correlated with depression and can lead to a decline in health-related quality of life and autonomic dysfunction. The prevalence of pain among Parkinson's patients ranges from 29% to 85% (Camacho-Conde & Campos-Arillo, 2020). Factors influencing quality of life in Parkinson's patients include concurrent depressive symptoms, disease severity and subtype, gait disturbances, medication side effects, and psychosocial dysfunction (Zhao et al., 2021). The Parkinson's Disease Questionnaire-39 (PDQ-39) is a disease-specific instrument used to assess quality of life in these patients (Schönenberg & Prell, 2022). Parkinson's patients experiencing pain tend to have worse PDQ-39 scores compared to those without pain, regardless of the type of pain experienced (Choi et al., 2017).

From a public health perspective, the importance of detecting and managing pain in Parkinson's patients becomes increasingly clear. Poorly managed pain can increase the economic burden on patients, their families, and the healthcare system as a whole, particularly considering the growing demand for long-term healthcare services (Valkovic et al., 2015). Additionally, prolonged pain can exacerbate the severity of both motor and non-motor symptoms, leading to greater disability and a further decline in quality of life (Politis et al., 2020).

Understanding the relationship between Parkinson's disease severity, pain, and quality of life can facilitate the development of more holistic and effective management strategies to improve quality of life and reduce pain in this population. This study aims to investigate the relationship between Parkinson's disease severity, pain, and quality of life in patients with Parkinson's disease.

METHOD

Research Design

This study employs an analytical research design with a cross-sectional approach. The research was conducted at Dr. Saiful Anwar General Hospital in East Java over six months, from October 2023 to March 2024, involving outpatients diagnosed with Parkinson's disease who reported pain. Purposive sampling was used to select subjects based on specific criteria relevant to the study's objectives. The study population included all patients diagnosed with Parkinson's who received outpatient care at Dr. Saiful Anwar General Hospital during the specified period.

Inclusion and Exclusion Criteria

The inclusion criteria included individuals diagnosed with Parkinson's disease according to Hughes criteria, Parkinson's patients experiencing pain, those aged 40 years and above, and individuals willing to participate in the study voluntarily. The exclusion criteria included individuals with moderate to severe cognitive impairment or psychiatric disorders that could affect their ability to provide accurate responses. Additionally, individuals unable to communicate effectively in the language of the study and those with pain due to cancer, autoimmune disease, or post-traumatic pain, as determined by anamnesis, were also excluded.

Severity Scale (Hoehn and Yahr Scale)

Stage I is characterized by symptoms and signs on one side of the body, with mild symptoms that are noticeable but do not interfere, usually involving tremors in one limb, and symptoms recognizable by close contacts such as friends. Stage II involves bilateral symptoms with minimal disability and postural or gait disturbance. Stage III is marked by significant slowing of body movements and balance impairment during walking or standing, indicating moderate general dysfunction. Stage IV indicates more severe symptoms, with patients only able to walk short distances, experiencing stiffness and bradykinesia, and unable to stand independently, with tremors possibly reduced compared to earlier stages. Stage V is the cachectic stage, where patients experience total disability, are unable to stand or walk, and require constant care (Hoehn & Yahr, 1967).

Pain Severity (Numeric Rating Scale/ NRS)

The NRS is widely used to assess self-reported pain intensity in children, although there is limited information on its psychometric properties for pain assessment. The NRS asks patients to rate their current, best, and worst pain levels in the past 24 hours on a scale from 0 (no pain) to 10 (worst imaginable pain) (Breivik et al., 2008; Bachruddin, 2016). Pain assessment using the NRS can be conducted verbally or in writing, with patients either stating (verbally) or marking (in writing) the number that best reflects their pain intensity. A score of 0 indicates "no pain," while a score of 10 indicates "worst possible pain." The scale facilitates easy pain evaluation and assessment (Bachruddin, 2016).

Quality of Life (Parkinson’s Disease Questionnaire-39 (PDQ-39)- INA Version)

The PDQ-39 is widely used to measure health-related quality of life (HRQoL) in patients, specifically for Parkinson's disease. Opara and colleagues validated the PDQ-39 as a reliable, sensitive, and specific instrument for this purpose. The PDQ-39 scoring system uses a 5-point ordinal scale, ranging from 0 (never) to 4 (always). The total score for each dimension ranges from 0 (never experiencing difficulty) to 100 (always experiencing difficulty), with lower total scores indicating better quality of life (Souza et al., 2007; Marinus et al., 2002; Schrag et al., 2000). The scale used is the Indonesian version of PDQ-39, validated by Oktariza et al. (Oktariza et al., 2009).

Dimension scores are calculated by dividing the total score by the maximum score and multiplying by 100. The overall score, known as the Parkinson's Disease Summary Index (PDSI) or PDQ-39 Summary Index (PDQ-39 SI), is calculated by averaging the dimension scores. Additionally, descriptive analysis using the cut-off point method determines the overall HRQoL profile. Based on ROC curve analysis, a cut-off point (COP) of 34.4 was identified, with 72.7% sensitivity and 84.2% specificity (Hendrik, 2013). Quality of life is considered good if the PDQ-39 score is ≤ COP and poor if the score is > COP.

Data Analysis

Demographic data including age, gender, disease duration, treatment type, pain type, and social activities, are presented descriptively, along with the number of Parkinson's patients with and without pain. Disease severity and pain scale are categorical independent variables, while quality of life is the numerical dependent variable. Relationships are analyzed using an independent t-test ($p < 0.05$), and risk factors are assessed via prevalence ratios. Multivariate regression is used to examine the combined effects of disease severity and pain on quality of life. Data analysis is performed using SPSS version 26 for Windows.

Ethics

This study is part of the research project "Factors Affecting the Quality of Life of Patients with Parkinson's Disease" and has received ethical approval from the Ethics Committee of Dr. Saiful Anwar General Hospital Malang, with the approval number 400/282/K.3/302/2023.

RESULT AND DISCUSSION

Result

In this study, 11 patients who met the inclusion and exclusion criteria during the study period were identified. The demographic characteristics of the study sample are detailed in Table 1 below. The clinical assessments of all participants are presented in Table 2.

Table 1. Demographic Characteristic of Study Participants

Characteristic		n	%
Age	40 - 50	2	18%
	51 - 60	3	27%
	61 - 70	2	18%
	71 - 80	4	36%
Gender	Female	7	64%
	Male	4	36%
Physical Activity	Actively walking independently	5	45%
	Walk with the help of family/caregiver	2	18%
	In bed (bedridden)	1	9%
	Depends on mobility aids	3	27%
Resting Tremor	Yes	11	100%
	No	0	0%
Tremor Dominant Side	Right	5	45%
	Left	6	55%
Non-Motor Symptoms	Anxiety	4	8%
	Depression	1	2%
	Dizzy when changing positions	1	2%
	Fatigue/get tired easily	8	17%
	Sleep Disorders (insomnia)	7	15%
	Gastrointestinal	5	10%
	Orthostatic hypotension	1	2%
	Nocturia	5	10%
	Painful	11	23%
	Constipation	5	10%
Parkinson's Treatment	Levodopa	3	27%
	Levodopa + Anticholinergic	4	36%
	LCE + Anticholinergic	1	9%
	LCE + Anticholinergic + Pramipexol	3	27%

Note: LCE: Levodopa/ Carbidopa/ Entacapone

Table 2. Parkinson's Assessment Results of Study Participants

Assessment Parkinson **(n=11)**		**n**	**%**
Subtype of PF	Akinetic rigid	4	36%
	Dominant tremor	7	64%
Bradykinesia Assessment	Finger tapping (+)	10	59%
	Masking face	7	41%
Rigidity	Cogwheel rigidity	4	36%
	Nothing	7	64%
Postural Instability	Arising from chair test (+)	2	18%
	Retropulsion (+)	4	36%
	Nothing	5	45%
Severity (Hoehn and Yahr)	1	3	27%
	2	2	18%
	3	2	18%
	4	2	18%
	5	2	18%

The Relationship Between Parkinson's Severity and Quality of Life Based on PDQ-39

Among the 11 participants, 5 had mild to moderate Parkinson's severity (Stages 1-2), with 2 (18.2%) showing good quality of life and 3 (27.3%) poor quality of life. In contrast, 6 participants had moderate to severe severity (Stages 3-5), with 1 (9.1%) reporting good quality of life and 5 (45.5%) poor quality of life. The PDQ-39 scores were normally distributed ($p = 0.679$) and homogeneous ($p = 0.942$). Independent T-Tests showed a significant association between PDQ-39 scores and Parkinson's severity ($p = 0.012$). The PDQ-39 questionnaire results are in Table 3, with pain scales detailed in Table 4.

Table 3. PDQ-39 Score Results for the Study Sample

Pts	Skor PDQ-39								
	A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**Total**
1	40	14	12	0	1	11	3	9	90
2	38	10	12	1	7	5	6	6	85
3	14	6	2	0	0	0	0	3	25
4	23	9	4	0	0	4	2	6	48
5	1	0	0	0	0	3	0	3	7
6	40	24	12	0	1	9	6	6	98
7	30	10	1	0	0	3	2	4	50
8	40	24	6	0	0	3	0	8	81
9	16	0	11	0	0	0	0	2	29
10	25	6	6	4	0	3	0	5	49
11	29	7	8	4	2	6	2	6	63
Average	26,9	10	6,73	0,8	1	4,2	1,9	5,2	56,8

Note: A: Mobility (maximum score 40); B: ADL (Activity Daily Life) [maximum score 24]; C: Emotional Health (maximum score 24); D: Stigma (maximum score 26); E: Social Support (maximum score 12); F: Cognition (maximum score 16); G: Communication (maximum score 12); H: Body Discomfort (maximum score 12).

Table 4. Results of Pain Assessment in Study Participants

Variable (n=11)	Description	n	%
Pain Scale (NRS)	2	1	9%
	3	5	45%
	4	2	18%
	5	3	27%
Pain Classification	Musculoskeletal	9	64%
	Neuropathic	5	36%
Diagnosis of Pain	CTS	1	7%
	LBP	1	7%
	Myalgia	6	43%
	OA	2	14%
	Polyneuropathic	4	29%

Note: NRS: Numeric Rating Scale; CTS: Carpal Tunnel Syndrome; LBP: Low Back Pain; OA: Osteoarthritis

The Relationship between NRS and Quality of Life based on PDQ-39

Pain severity on the Numeric Rating Scale (NRS) for Parkinson's disease was categorized as mild (1-3), moderate (4-6), and severe (>7). Among the 6 participants with mild pain, 2 (18.2%) had a good quality of life, while 4 (36.4%) had a poor quality of life. Of the 5 participants with moderate pain, 1 (9.1%) had a good quality of life, and 4 (36.4%) had a poor quality of life. No participants were classified as having severe pain. The Shapiro-Wilk test confirmed the normality of PDQ-39 scores ($p = 0.679$), and Levene's test confirmed homogeneity ($p = 0.164$).

Parametric Independent T-Tests revealed no significant association between PDQ-39 scores and pain severity ($p = 0.117$), with mean PDQ-39 scores of 44.0 ± 14.310 for mild pain and 72.2 ± 36.995 for moderate pain.

The Relationship Between Parkinson's Severity and NRS

A Pearson correlation analysis between Parkinson's severity scores and pain severity scores yielded a correlation coefficient of 0.461 with a p-value of 0.154 ($p > 0.05$), indicating no significant relationship between Parkinson's severity and pain severity. Therefore, it can be concluded that the degree of Parkinson's severity does not correlate with the degree of pain severity.

Discussion

Parkinson's disease (PD) classification often hinges on the age of onset, categorizing patients into distinct groups based on when symptoms first appear. Research has shown that an older age at onset is associated with more severe motor and non-motor symptoms. The typical presentation includes a combination of motor symptoms such as bradykinesia, resting tremor, and rigidity, with rigidity being more prevalent among younger onset cases (under 50 years). Approximately 80% of patients with localized onset primarily exhibit symptoms in their upper limbs. While symptom presentations are generally similar across different age groups, the severity of both motor and non-motor features tends to increase with older onset age (Pagano et al., 2016).

In a descriptive cross-sectional study conducted at neurology clinics, patients with Parkinson's disease had an average age of 61.87 years, with a predominance of males (72.3%) (Haeriyoko et al., 2018). Another study reported that most patients fell within the 60-79 age range, with the majority classified in Hoehn and Yahr stages I & II (Setiarini, 2018). Additionally, early-onset Parkinson's disease (EOPD) refers to cases where symptoms appear before the age of 50, characterized by distinct clinical, pathological, and genetic features compared to those with later onset. This differentiation underscores the need for personalized, multidisciplinary management approaches (Mehanna et al., 2022; Morales-Briceño et al., 2020; Post et al., 2020).

Non-motor symptoms are also prevalent, with pain affecting a significant majority of patients and linked to central abnormalities in pain processing (Buhmann et al., 2020). Our research findings indicate that among patients aged 40-50 years, mobility was the most affected dimension on the PDQ-39 questionnaire, followed by emotional health, activities of daily living (ADL), and bodily discomfort. Similarly, in the 51-60 age group, mobility was predominantly affected, followed by ADL, emotional health, bodily discomfort, and cognition. Patients aged 61-70 years also showed consistent disturbances in mobility, ADL, emotional health, bodily discomfort, and cognition. Among patients over 70 years old, mobility, ADL, emotional health, bodily discomfort, and cognition were sequentially the most disrupted dimensions. These findings highlight significant shifts in dimensions among early-onset Parkinson's disease (EOPD) patients. Those under 50 years old, classified as EOPD, commonly experience declines in emotional health, paralleling previous studies that indicate poorer quality of life measured by PDQ-39 in younger onset patients compared to older onset ones. Additionally, younger onset patients more frequently encounter depression. Differences in coping strategies and satisfaction with emotional support between the two groups did not reach significance. Younger onset patients also more commonly face job loss, family life disturbances, heightened stigma, and depression compared to older onset PD patients. Apart from more severe motor complications related to treatment, social and psychosocial factors may significantly contribute to reduced quality of life in younger PD patients (Schrag et al., 2017).

In prior U.S. studies, PDQ-39 has proven effective for assessing the quality of life in Parkinson's patients. Patients found it helpful for remembering discussions with healthcare providers, formulating specific questions, and identifying factors affecting their quality of life. Caregivers gained insights into daily patient needs, while neurologists reported more efficient discussions focused on patient concerns. Additional healthcare providers noted that PDQ-39 subdomain scores provided a holistic view, aiding in setting short- and long-term goals (Neff et al., 2018). A cross-sectional study compared quality of life between Tremor Dominant (TD) and Postural Instability Gait Difficulty (PIGD) subtypes at neurological clinics in Indonesia. TD subtype patients generally reported a better quality of life than PIGD subtype patients, particularly in mobility and activities of daily living (Anindyta & Sutarni, 2020). Research at Rumah Sakit Haji Adam Malik Medan highlighted a strong association between disease severity and quality of life in Parkinson's patients. Those on polytherapy generally reported lower quality of life scores compared to monotherapy, emphasizing the impact of medication quantity on patient well-being (Heidiyana et al., 2023). In previous studies, tremor amplitude showed significant correlations with daily activities, emotional well-being, stigma, and social support as measured by PDQ-39. Grip and pinch strengths also correlated significantly with various PDQ-39 parameters, underscoring their relevance in assessing Parkinson's symptoms (Kilinc et al., 2023). Our study found that reduced mobility significantly affects activities of daily living in Parkinson's patients, impacting their overall quality of life. Emotional health in Parkinson's patients is notably affected by mobility limitations, potentially leading to feelings of frustration, helplessness, and social isolation. Stigma related to mobility issues can further exacerbate emotional distress and hinder social support networks (Jin et al., 2017; Masaki et al., 2023). Contrasting our findings, a study of 161 PD patients assessed pain using patient descriptions, structured interviews, and detailed neurological examinations, with quality of life evaluated using PDQ-39. Seventy-four-point five percent of patients experienced chronic pain, predominantly musculoskeletal, followed by radicular/neuropathic, dystonic, and central pain. PD patients with pain had worse PDQ-39 scores compared to those without pain. Multivariate regression analysis adjusted for disease-related factors and motor characteristics identified younger onset age, high Unified Parkinson’s Disease Rating Scale scores, Beck Depression Inventory, and Visual Analogue Scale scores as significant predictors of poor PDQ-39 scores. Pain, along with depression, poor daily activities, and younger onset age, correlated with poor quality of life. All pain types affected PD patients' quality of life, underscoring the need to consider pain management in PD care (Choi et al., 2017). In our study, no significant relationship was found between pain based on NRS and PDQ-39 scores. However, this raises questions about factors affecting these results, such as the sample size, individual pain responses, and the sensitivity of measurement methods. Additionally, unaccounted confounding factors, like previous analgesic use, could influence our findings. Further research is needed to clarify the relationship between pain and quality of life in Parkinson's patients.

In a previous study involving 250 Parkinson's disease patients, where 70% were in mild to moderate stages, the average age was 67.4 years with an average disease duration of 7.1 years. The prevalence of pain was high (82%), mostly linked to Parkinson's disease. Pain duration correlated with the frequency of intense pain (R: 0.393; $p < 0.05$). Electric shock-like pain was the most common sensation (64%), differing from other studies where burning and itching were more frequently reported. This study confirms various aspects of pain experience in Parkinson's, including its evolution over time and its association with disease characteristics and gender differences (Camacho-Conde & Campos-Arillo, 2020). Another study reported pain in 79.3% of Parkinson's patients, predominantly musculoskeletal (70.1%), nocturnal (43.9%), radicular (43.0%), chronic (42.1%), fluctuation-related (34.6%), and orofacial pain (16.8%). Most patients (74.8%) experienced multiple types of pain. Fluctuation-related and orofacial pain were notably more common in patients with advanced Parkinson's stages (3–5) compared to earlier stages (1–2). Pain severity correlated independently with age, depression severity, perceptual issues, and sexual function. These findings highlight the complex nature of pain in Parkinson's disease and its impact on patients' quality of life (Hoang et al., 2023).

Study Limitations

One limitation of this study is the relatively small sample size, with only 11 participants. This limitation is primarily due to the low prevalence of pain among Parkinson's disease patients in RSU Dr. Saiful Anwar, which restricted the number of eligible cases. However, despite the small sample size, the study's findings remain significant and meaningful for several reasons.

Firstly, the study focuses on a specific and well-defined population, allowing for an in-depth analysis of the relationship between Parkinson's disease severity, pain intensity, and quality of life. The homogeneity of the sample, confirmed through tests of normality and homogeneity, ensures that the data collected is consistent and reliable. Additionally, the study was able to demonstrate statistically significant results in key areas, highlighting the robustness of the observed effects.

Lastly, while the small sample size may limit the generalizability of the findings, the results provide valuable insights that can serve as a foundation for future research with larger cohorts. This study contributes meaningfully to the existing literature by emphasizing the importance of pain management in Parkinson's disease and its impact on quality of life.

CONCLUSION

This study found a significant correlation ($p < 0.05$) between Parkinson's disease severity and quality of life, indicating that as the disease progresses, various aspects of quality of life—physical, emotional, and social—are notably impacted. However, no significant correlation ($p > 0.05$) was observed between pain severity and quality of life, suggesting that while pain is common in Parkinson's disease, its intensity may not directly affect overall quality of life measures. These findings highlight the need for targeted interventions that address both disease severity and quality of life. Future research should explore additional factors influencing these relationships to improve Parkinson's disease management and patient well-being.

ACKNOWLEDGEMENT

This research was funded by the Faculty of Medicine, Universitas Brawijaya.

REFERENCES

Andrew, A. S., Anderson, F. L., Lee, S. L., et al. (2021). Lifestyle factors and Parkinson’s disease risk in a rural New England case-control study. *Parkinson’s Disease*, 2021, 1–7. https://doi.org/10.1155/2021/5546817

Anindyta, M. A., & Sutarni, S. (2020). Perbandingan kualitas hidup pasien Parkinson subtipe tremor dominant dan postural instability gait disorder. *Callosum Neurology Journal*, 3(1), 35–42.

Buhmann, C., Kassubek, J., & Jost, W. H. (2020). Management of pain in Parkinson’s disease. *Journal of Parkinson's Disease*, 10(S1), S37–S48. https://doi.org/10.3233/JPD-202072

Camacho-Conde, J. A., & Campos-Arillo, V. M. (2020). The phenomenology of pain in Parkinson’s disease. *Korean Journal of Pain*, 33(1), 90–96. https://doi.org/10.3344/kjp.2020.33.1.90

Choi, S.-M., Kim, B. C., Jung, H.-J., et al. (2017). Impact of pain and pain subtypes on the quality of life of patients with Parkinson’s disease. *Journal of Clinical Neuroscience*, 45, 105–109. https://doi.org/10.1016/j.jocn.2017.06.004

Emamzadeh, F. N., & Surguchov, A. (2018). Parkinson’s disease: Biomarkers, treatment, and risk factors. *Frontiers in Neuroscience*, 12, 612. https://doi.org/10.3389/fnins.2018.00612

Haeriyoko, W. A., Samatra, D. P., GS, S. Y. T., et al. (2018). Profil gangguan tidur penderita Parkinson di rumah sakit rujukan di Kota Denpasar tahun 2018. *Callosum Neurology Journal*, 3(1), 1–10.

Heidiyana, M., Surbakti, K. P., & Hutagalung, H. S. (2023). The association between degree of severity and number of medications with quality of life in Parkinson’s disease patients. *Journal of Society Medicine*, 2(3), 103–112. https://doi.org/10.31228/josmed-2023-021

Hoang, D. T., Xing, F., Nguyen, T. D., et al. (2023). Pain is common in early onset Parkinson’s disease and pain severity is associated with age and worsening of motor and non-motor symptoms.

Journal of Neurological Sciences, 455, 122784. https://doi.org/10.1016/j.jns.2023.122784

Hoehn, M. M., & Yahr, M. D. (1967). Parkinsonism: onset, progression, and mortality. *Neurology*, 17(5), 427–442. https://doi.org/10.1212/WNL.17.5.427

Jin, Y., Mao, Z., Ling, Z., et al. (2017). Altered emotional recognition and expression in patients with Parkinson’s disease. *Neuropsychiatric Disease and Treatment*, 13, 2891–2902. https://doi.org/10.2147/NDT.S147508

Kilinc, B., Cetisli-Korkmaz, N., Bir, L. S., et al. (2023). The quality of life in individuals with Parkinson’s disease: Is it related to functionality and tremor severity? A cross-sectional study. *Physiotherapy Theory and Practice*, 1–10. https://doi.org/10.1080/09593985.2023.2214349

Marino, B. L. B., de Souza, L. R., Sousa, K. P. A., et al. (2020). Parkinson’s disease: A review from pathophysiology to treatment. *Mini-Reviews in Medicinal Chemistry*, 20(8), 754–767. https://doi.org/10.2174/138955752066619112745941

Masaki, M., Takeuchi, M., Kasahara, M., et al. (2023). Association of activities of daily living, mobility and balance ability, and symptoms of Parkinson’s disease with the masses and amounts of intramuscular non-contractile tissue of the trunk and lower extremity muscles in patients with Parkinson’s disease. *Journal of Medical Ultrasonics*, 50(4), 551–560. https://doi.org/10.1007/s10396-023-01219-1

Mehanna, R., Smilowska, K., Fleisher, J., et al. (2022). Age cutoff for early-onset Parkinson’s disease: Recommendations from the International Parkinson and Movement Disorder Society Task Force on Early Onset Parkinson’s Disease. *Movement Disorders Clinical Practice*, 9(6), 869–878. https://doi.org/10.1002/mdc3.13477

Morales-Briceño, H., Mohammad, S. S., Post, B., et al. (2020). Clinical and neuroimaging phenotypes of genetic parkinsonism from infancy to adolescence. *Brain*, 143(3), 751–770. https://doi.org/10.1093/brain/awaa032

Neff, C., Wang, M. C., & Martel, H. (2018). Using the PDQ-39 in routine care for Parkinson’s disease. *Parkinsonism & Related Disorders*, 53, 105–107. https://doi.org/10.1016/j.parkreldis.2018.05.009

Oktariza, Y., Amalia, L., Sobaryati, & Kurniawati, M. Y. (2019). Evaluasi kualitas hidup pasien Parkinson berdasarkan terapi berbasis Levodopa. *Jurnal Farmasi Klinik Indonesia*, 8(4), 246–255. https://doi.org/10.15416/ijcp.2019.8.4.246

Pagano, G., Ferrara, N., Brooks, D. J., et al. (2016). Age at onset and Parkinson disease phenotype. *Neurology*, 86(14), 1400–1407. https://doi.org/10.1212/WNL.0000000000002461

Pereira, M. G., Carvalho, C., Costa, E. C. V., et al. (2021). Quality of life in chronic pain patients: Illness- and wellness-focused coping as moderators. *Psych Journal*, 10(2), 283–294. https://doi.org/10.1002/pchj.440

Politis, M., Wu, K., Molloy, S., Bain, P., Chaudhuri, K. R., & Piccini, P. (2020). Parkinson's disease symptoms: The patient’s perspective. *Movement Disorders*, *35*(1), 120-128. https://doi.org/10.1002/mds.23862

Post, B., van den Heuvel, L., van Prooije, T., et al. (2020). Young onset Parkinson’s disease: A modern and tailored approach. *Journal of Parkinson's Disease*, 10(S1), S29–S36. https://doi.org/10.3233/JPD-202072

Schönenberg, A., & Prell, T. (2022). Measuring quality of life with the Parkinson’s Disease Questionnaire-39 in people with cognitive impairment. *PLoS ONE*, 17(3), e0266140. https://doi.org/10.1371/journal.pone.0266140

Schrag, A., Hovris, A., Morley, D., et al. (2017). Young- versus older-onset Parkinson’s disease: Impact of disease and psychosocial consequences. *Movement Disorders*, 18(11), 1250–1256. https://doi.org/10.1002/mds.10578

Setiarini, R. (2018). Profil pasien Parkinson di poliklinik saraf RSUP Dr. Sardjito. *Fakultas Kedokteran Universitas Gadjah Mada*. [Unpublished manuscript].

Tambun, O., Marisdina, S., & Bahar, E. (2021). Faktor-faktor yang mempengaruhi kualitas hidup penderita penyakit Parkinson dengan menggunakan. *Unpublished manuscript*.

Valkovic, P., Minar, M., Singliarova, H., Harsany, J., Hanakova, M., & Martinkova, J. (2015). Pain in Parkinson’s disease: A cross-sectional study of its prevalence, types, and relationship to depression and quality of life. *PloS one*, *10*(8), e0136541. https://doi.org/10.1371/journal.pone.0136541

Young Blood, M. R., Ferro, M. M., Munhoz, R. P., et al. (2016). Classification and characteristics of pain associated with Parkinson’s disease.

Parkinson's Disease, 2016, 1–8. https://doi.org/10.1155/2016/6067132

Zhao, N., Yang, Y., Zhang, L., et al. (2021). Quality of life in Parkinson's disease: A systematic review and meta-analysis of comparative studies. *CNS Neuroscience & Therapeutics*, 27(3), 270–279. https://doi.org/10.1111/cns.13531