ORIGINAL ARTICLE

Influence of *Helicobacter pylori* Eradication on Motor Fluctuation Patterns in Advanced Parkinson's Disease: A Quasi-experimental Evaluation Using MDS-Unified Parkinson's Disease Rating Scale

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Abstract

Background: Parkinson's disease (PD) represents a major neurodegenerative condition globally, and its contribution to the overall neurological disease burden is expected to rise markedly by 2040. Motor complications, including wearing-off phenomena, on-off fluctuations, and dyskinesias, remain major therapeutic challenges in advanced PD. Emerging evidence suggests that *Helicobacter pylori* infection may worsen motor symptoms by impairing gastrointestinal absorption of levodopa. **Methods:** This prospective quasi-experimental investigation was carried out at Saveetha Medical College and Hospital over a 12-month period, from January to December 2024. The study included 20 individuals diagnosed with advanced PD who experienced motor response fluctuations. Patients confirmed to be *H pylori* positive through endoscopic biopsy or stool antigen assessment were treated with an eradication regimen consisting of amoxicillin 500 mg thrice daily for 1 week and vonoprazan 20 mg once daily for 2 weeks. Motor performance was evaluated with the MDS-unified PD rating scale (UPDRS) Part III scale before treatment and during follow-up visits at 6 and 12 weeks after therapy. **Results:** The eradication rate was 70%. Compared with patients without infection, those with *H. pylori* positivity belonged to an older age group and developed PD at a significantly later age ($P < 0.05$). MDS-UPDRS Part III scores improved significantly following eradication therapy, particularly in the OFF medication state. Lifestyle factors, including smoking and dietary intake, were not significantly associated with treatment outcomes. The observed results indicate that *H. pylori* infection may be linked to poorer motor regulation in PD, while eradication treatment may lessen fluctuation severity by enhancing the availability of absorbed levodopa. **Conclusion:** Treatment aimed at eliminating *H. pylori* may offer motor benefit in advanced PD by improving the gastrointestinal handling and absorption of levodopa. Larger multicenter studies with microbiological confirmation of eradication and longer follow-up are required to validate these findings and further explore gut-brain axis mechanisms. Region-specific eradication protocols considering antimicrobial resistance patterns are also warranted.

Key words: *Helicobacter pylori*, levodopa, microbiota-gut-brain axis, motor fluctuations, Parkinson's disease, unified Parkinson's disease rating scale

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INTRODUCTION

Parkinson's disease (PD) is a major neurodegenerative disorder and ranks next to Alzheimer's disease in global prevalence.[1] As populations age and survival increases, neurodegenerative conditions are expected to place an increasing burden on health-care systems worldwide. It has been projected that by 2040, neurodegenerative disorders, including PD and Alzheimer's disease, may account for a larger proportion of global deaths than many currently dominant causes, including cancer.[2] This anticipated rise highlights the need to address neurodegenerative diseases as an expanding public health priority. The 2015 Global Burden of Disease analysis reported that PD showed one of the most rapid increases among neurological disorders with respect to prevalence and disability burden.[3] This rising trend may be attributed to ageing populations, improved disease recognition, greater awareness, and advances in diagnostic methods. Even with improved recognition and diagnosis, treating PD remains difficult because the disease progresses gradually, presents differently among patients, and is often complicated by both motor and non-motor features.

The clinical manifestations of PD vary widely between individuals and may also fluctuate as the disease advances in the same patient. Frequently encountered motor complications include wearing-off episodes, unpredictable ON-OFF responses, and levodopa-induced dyskinesias. These complications may be affected by multiple variables, such as levodopa dose and treatment duration, age at onset, stress, sleep pattern, dietary factors, and patient-specific differences in drug handling and response. Although levodopa remains the most effective pharmacological option for controlling PD motor symptoms, prolonged therapy is commonly associated with treatment-related motor complications. These complications are particularly common in patients who develop PD at a young age and who are treated with levodopa for a long time. The assessment of these motor complications is particularly challenging considering the marked heterogeneity of PD presentation and progression.[4] Clinical researchers often use patient-reported daily diaries to track and assess treatment outcomes. These diaries serve to monitor the effectiveness of different medical and surgical interventions in reducing motor fluctuations and dyskinesias.

Among dyskinesias in PD, peak-dose dyskinesia is the most commonly observed pattern and usually occurs when circulating levodopa concentrations reach their maximum level. It is usually characterized by involuntary, repetitive, choreic (dance-like) or ballistic (jerking) movements of the head, trunk, and limbs, and sometimes even of the respiratory muscles. Less common symptoms include tremors and punding, a compulsive, repetitive behavior. In addition, patients with diphasic dyskinesias or wearing-off effects often have dystonia (prolonged muscle contractions that cause abnormal postures). It is important to understand the full clinical spectrum of these motor problems for optimizing patient care and outcomes.[5]

While PD is classically defined by its motor features, non-motor manifestations also contribute substantially to patient disability and overall disease burden.[6] Gastrointestinal involvement is one of the common non-motor manifestations of PD and, in some patients, may appear years before the development of typical motor signs. Constipation is frequently reported in PD and has also been linked with a higher subsequent risk of PD. Such findings have encouraged further investigation into the possible contribution of gut-related mechanisms to the onset and progression of PD.

Current research increasingly indicates that communication between the gut microbiota and the brain may be involved in the biological mechanisms underlying PD. Changes in intestinal microbiota, gut inflammation, and disruption of the intestinal barrier may promote neuroinflammation and contribute to progressive neurodegenerative changes. In addition, the reported association of chronic constipation and inflammatory bowel disease with increased PD risk further strengthens the concept that gastrointestinal factors may influence disease initiation and progression.[7,8]

Helicobacter pylori (HP) is a Gram-negative organism that commonly colonizes the stomach and can produce persistent gastric mucosal inflammation. It is associated with several gastrointestinal disorders, including peptic ulcers, gastroduodenitis, and more severe conditions such as gastric cancer.[9] Accumulating evidence suggests a possible relationship between long-standing HP infection and increased susceptibility to PD. Meta-analytic evidence indicates that HP infection is detected more frequently among patients with PD than in the general population. Furthermore, PD patients infected with HP tend to have poorer motor control than those who are not infected.[10] It is possible that HP infection affects gastrointestinal function and interferes with levodopa absorption, reducing its efficacy and worsening motor symptoms. As levodopa needs to be properly absorbed by the GI tract to work, it is very much affected if this process gets disturbed.

Eradication of HP may have clinical benefits given the impact of gastrointestinal dysfunction on PD progression and symptom management. Eradication consists of a combination of antibiotics and acid-suppressing drugs and has been successful in most patients. Eradication of HP may improve control of motor symptoms by improving gut health and potential for improved levodopa absorption. Therefore, this study was planned to evaluate whether HP eradication therapy influences motor fluctuations in patients with advanced PD. Changes in unified PD rating scale (UPDRS) scores were used to assess clinical response and to explore the relevance of gastrointestinal factors in PD management.

METHODS

A prospective quasi-experimental study was undertaken in the Department of Internal Medicine, Saveetha Medical College and Hospital, over a 1-year period from January 2024 to December 2024. The study followed a single-arm, open-label design and aimed to evaluate the effect of *H. pylori* eradication therapy on motor fluctuations in patients with PD. Based on power calculation, 10 participants were required to detect a meaningful reduction in motor fluctuations.

Patients were eligible if they were 50–80 years of age, had advanced PD with motor fluctuations, particularly the "on-off" phenomenon, and were confirmed to have *H. pylori* infection by urea breath test, stool antigen test, or upper gastrointestinal endoscopy. Patients were not included if they had previously received eradication treatment for *H. pylori*, had used proton pump inhibitors for more than 4 weeks before enrolment, had gastrointestinal ulcer disease or malignancy, or had severe cognitive dysfunction, defined as a mini-mental state examination score of <24. Consecutive patients fulfilling the selection criteria were screened by a movement disorder specialist. The study procedure is summarized in [Figure 1].

MDS- UPDRS Part III was used for evaluating motor symptoms [Figure 2]. The intervention involved a newly implemented *H. pylori* eradication regime which includes tablet amoxicillin 500 mg thrice daily for 7 days and tablet vonopraxon 40 mg once daily for 14 days. Confirmation of successful eradication was conducted at 6 weeks post-treatment.

Motor function was evaluated again at 6 weeks and 12 weeks after treatment using MDS-UPDRS Part III, as illustrated in the sample assessment sheet in Figure 3. Statistical analysis was performed with the Statistical Package for the Social Sciences version 26. Patient characteristics and baseline findings were described using appropriate summary measures. Pre- and post-treatment changes in MDS-UPDRS Part III scores were tested using either the paired t-test or Wilcoxon signed-rank test, depending on whether the data followed a normal distribution. Results with *P* value below 0.05 were regarded as statistically significant.

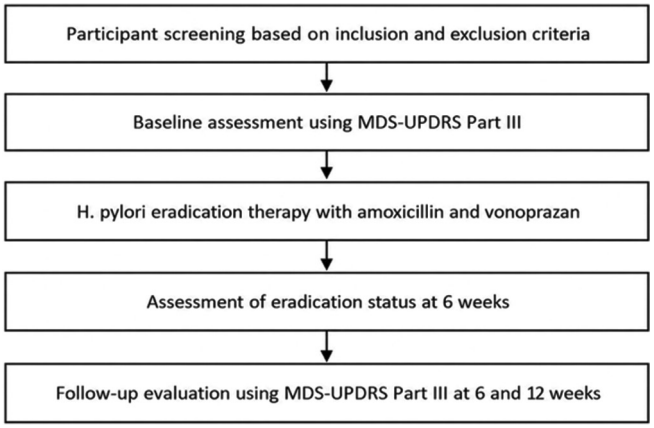

Figure 1: Flowchart showing the methodology of the study

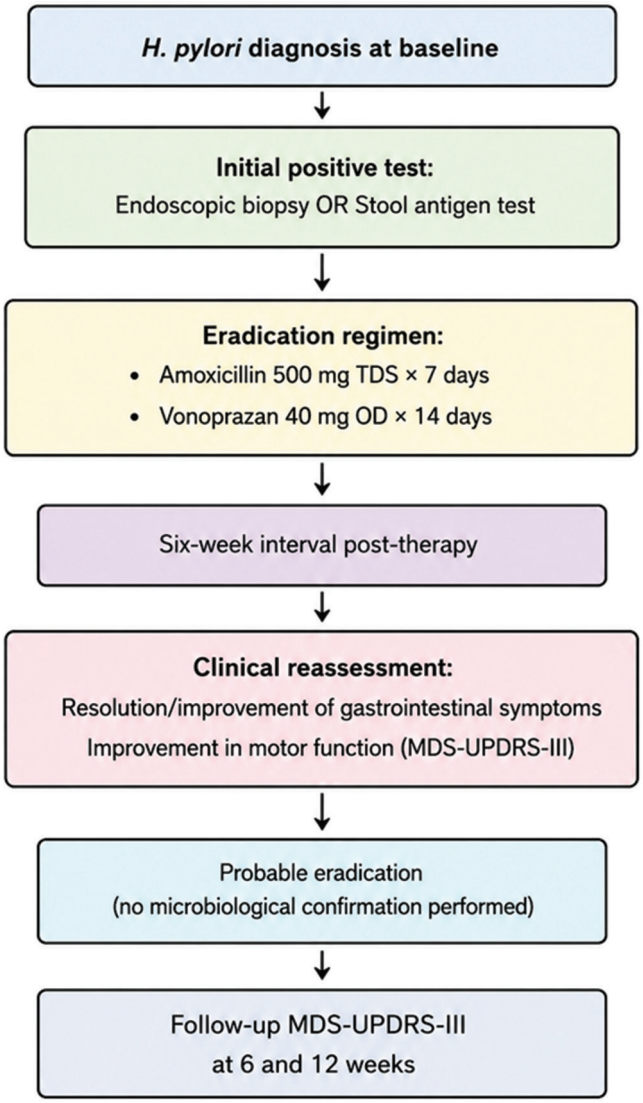

Figure 2: Flowchart showing *Helicobacter pylori* diagnosis, eradication regimen, and follow-up assessments in the study

RESULTS

Study population and *H. pylori* status

The study included 20 individuals with advanced PD who experienced motor fluctuations. Half of the participants tested positive for *H. pylori*, while the other half showed no evidence of infection. Among the infected participants, diagnosis was established by endoscopic biopsy in six cases and by stool antigen testing in four cases. Histopathological images from representative *H. pylori*-positive cases are shown in Figure 4.

Patient Name or Subject ID | Site ID | (mm-dd-yyyy) Assessment Date | Investigator's Initials

MDS UPDRS Score Sheet

1.A	Source of information	☐ Patient ☐ Caregiver ☐ Patient + Caregiver	3.3b	Rigidity– RUE	
			3.3c	Rigidity– LUE	
Part I			3.3d	Rigidity– RLE	
1.1	Cognitive impairment		3.3e	Rigidity– LLE	
1.2	Hallucinations and psychosis		3.4a	Finger tapping– Right hand	
1.3	Depressed mood		3.4b	Finger tapping– Left hand	
1.4	Anxious mood		3.5a	Hand movements– Right hand	
1.5	Apathy		3.5b	Hand movements– Left hand	
1.6	Features of DDS		3.6a	Pronation- supination movements– Right hand	
1.6a	Who is filling out questionnaire	☐ Patient ☐ Caregiver ☐ Patient + Caregiver	3.6b	Pronation- supination movements– Left hand	
			3.7a	Toe tapping– Right foot	
1.7	Sleep problems		3.7b	Toe tapping– Left foot	
1.8	Daytime sleepiness		3.8a	Leg agility– Right leg	
1.9	Pain and other sensations		3.8b	Leg agility– Left leg	
1.10	Urinary problems		3.9	Arising fromchair	
1.11	Constipation problems		3.10	Gait	
1.12	Light headedness on standing		3.11	Freezing of gait	
1.13	Fatigue		3.12	Postural stability	
Part II			3.13	Posture	
2.1	Speech		3.14	Global spontaneity of movement	
2.2	Saliva and drooling		3.15a	Postural tremor– Right hand	
2.3	Chew ing and sw allowing		3.15b	Postural tremor– Left hand	
2.4	Eating tasks		3.16a	Kinetic tremor– Right hand	
2.5	Dressing		3.16b	Kinetic tremor– Left hand	
2.6	Hygiene		3.17a	Rest tremor amplitude– RUE	
2.7	Handw riting		3.17b	Rest tremor amplitude– LUE	
2.8	Doing hobbies and other activities		3.17c	Rest tremor amplitude– RLE	
2.9	Turning in bed		3.17d	Rest tremor amplitude– LLE	
2.10	Tremor		3.17e	Rest tremor amplitude– Lip/jaw	
2.11	Getting out of bed		3.18	Constancy of rest tremor	
2.12	Walking and balance			Were dyskinesias present?	☐ No ☐ Yes
2.13	Freezing			Did these movements interfere w ith ratings?	☐ No ☐ Yes
3a	Is the patient on medication?	☐ No ☐ Yes		Hoehn and Yahr Stage	
3b	Patient's clinical state	☐ Off ☐ On	**Part IV**		
3c	Is the patient on levodopa?	☐ No ☐ Yes	4.1	Time spent w ith dyskinesias	
3.C1	If yes, minutes since last dose:		4.2	Functional impact of dyskinesias	
Part III			4.3	Time spent in the OFF state	
3.1	Speech		4.4	Functional impact of fluctuations	
3.2	Facial expression		4.5	Complexity of motor fluctuations	
3.3a	Rigidity– Neck		4.6	Painful OFF-state dystonia	

Figure 3: MDS unified Parkinson's disease rating scale-III score sheet used to assess motor fluctuations among study subjects

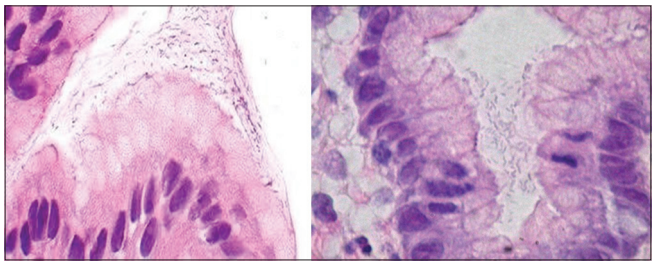

Figure 4: Histopathological images of *Helicobacter pylori*-positive study subjects

Baseline demographic and clinical characteristics

Table 1 presents the baseline demographic and clinical profile of the study participants. Patients with *H. pylori* infection were older than those without infection, with mean ages of 63.3 ± 5.7 years and 52.5 ± 9.7 years, respectively. Age at onset of PD was also higher in the *H. pylori*-positive group compared with the *H. pylori*-negative group.

Table 1: Demographic and baseline characteristics of the study participants according to HP status

Variables	HP positive (10)	HP negative (10)	Total	*P*-value
Gender				
Male	5	6	11	0.635
Age (years)	63.3±5.7	52.5±9.7	57.9±11.5	<0.01
Age (at onset)	55.6±4.3	52.2±8.9	55.4±8.7	<0.01
Smoking	3	3	6	0.531
No of fruits or vegetable intake/day	2.2±0.5	2.3±0.6	2.25±0.8	0.175
Disease duration in years	7.8±4.8	7.9±3.6	11.8±4.2	0.567

HP: *Helicobacter pylori*

No significant association was observed between *H. pylori* status and other baseline variables, including gender, smoking history, fruit and vegetable intake, or duration of PD. These findings indicate that, in the present cohort, older age and later disease onset were the principal baseline characteristics associated with *H. pylori* positivity.

Baseline MDS-UPDRS Part III scores according to *H. pylori* status

Motor severity at baseline was measured with the MDS-UPDRS Part III during both OFF and ON treatment conditions. Table 2 shows that participants with *H. pylori* infection had greater motor impairment than participants without infection.

During the OFF state, the average MDS-UPDRS Part III score was 60.8 ± 2.5 among infected patients, compared with 30.7 ± 3.6 among those who were *H. pylori* negative. A similar pattern was observed in the ON state, where scores were higher in the *H. pylori*-positive group than in the negative group, 42.5 ± 4.7 versus 21.5 ± 5.4, respectively. These findings suggest that the presence of *H. pylori* infection was linked to poorer motor performance during both medication phases.

Changes in MDS-UPDRS Part III scores following *H. pylori* eradication therapy

Among *H. pylori*-positive patients, MDS-UPDRS Part III scores showed improvement following eradication therapy. As shown in [Table 3], the mean OFF-state score decreased from 60.8 ± 2.5 before treatment to 54.1 ± 4.7 after treatment, and this reduction was statistically significant. Similarly, the mean ON-state score declined from 42.5 ± 4.7 to 40.3 ± 1.8 after therapy, also demonstrating a statistically significant improvement.

The reduction was more pronounced in the OFF medication state than in the ON medication state. This suggests that *H. pylori* eradication therapy may be particularly beneficial in reducing baseline motor impairment and OFF-period severity in patients with advanced PD.

Table 2: Baseline MDS-UPDRS Part III scores during OFF and ON medication states according to HP status

Variable	HP positive (10)	HP negative (10)	*P*-value
Off UPDRS score	60.8±2.5	30.7±3.6	<0.01
On UPDRS score	42.5±4.7	21.5±5.4	<0.01

HP: *Helicobacter pylori*, UPDRS: Unified Parkinson's disease rating scale

Table 3: Changes in MDS-UPDRS Part III scores before and after HP eradication therapy among HP-positive patients

Variable	Before HP eradication	After HP eradication	*P*-value
Off UPDRS score	60.8±2.5	54.4±4.7	0.01
On UPDRS score	42.5±4.7	40.3±1.8	0.04

HP: *Helicobacter pylori*, UPDRS: Unified Parkinson's disease rating scale

Individual patient-level changes after eradication therapy

Figure 5 illustrates the patient-wise variation in MDS-UPDRS Part III scores recorded before and after *H. pylori* eradication treatment. After treatment, motor scores decreased in the majority of patients. This reduction was more prominent during the OFF state, indicating improvement in underlying motor performance and a decrease in the severity of OFF episodes. A mild improvement was also observed in the ON medication state, indicating a possible improvement in therapeutic response after eradication therapy.

Overall, the results indicate that eliminating *H. pylori* infection may help reduce motor fluctuations in advanced PD, possibly by enhancing gastrointestinal function and improving levodopa absorption.

Overall, *H. pylori* infection was detected in half of the patients included in the study, indicating a considerable burden of infection among individuals with advanced PD and motor fluctuations. Patients who were positive for *H. pylori*

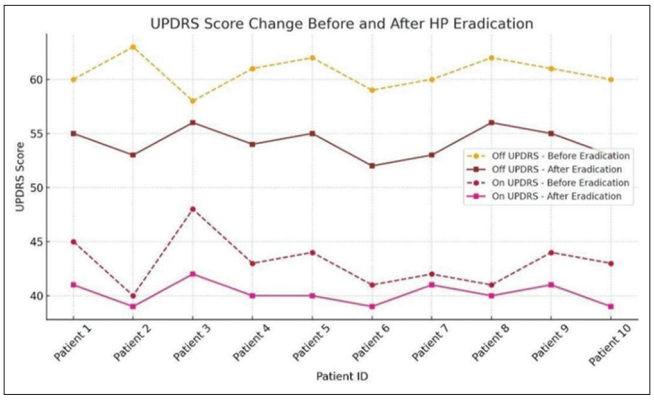

Figure 5: Individual changes in MDS-unified Parkinson's disease rating scale part III scores before and after *Helicobacter pylori* eradication therapy

differed from the non-infected group in important baseline characteristics, particularly with respect to age and age at disease onset. The infected patients were older and showed a later onset of PD, suggesting that *H. pylori* positivity in this cohort was more frequently observed in the older patient subgroup. In addition, baseline motor assessment demonstrated greater impairment among *H. pylori*-positive patients, as reflected by higher MDS-UPDRS Part III scores in both OFF and ON medication states. This pattern indicates that the presence of *H. pylori* infection may be associated with more severe motor dysfunction irrespective of medication state.

Following eradication therapy, significant improvement was observed in both OFF-state and ON-state motor scores, with a greater reduction in the OFF state. These findings suggest that *H. pylori* infection may contribute to worsening motor fluctuations in advanced PD and that eradication therapy may offer potential clinical benefit as an adjunctive treatment strategy.

DISCUSSION

Growing evidence suggests that *H. pylori* infection may interfere with the therapeutic response to levodopa in patients with PD, particularly by contributing to early or unpredictable "OFF" episodes. Several mechanisms may explain this association. Chronic *H. pylori*-related gastritis can alter gastric acidity, delay gastric emptying, and affect the intestinal handling of orally administered levodopa. Since levodopa is primarily absorbed in the proximal small intestine, disturbances in gastric transit and mucosal function may reduce or delay its availability at the absorption site. This can result in variable plasma levodopa levels and may contribute to motor fluctuations, especially early morning OFF states and post-dose wearing-off episodes. These effects are clinically important because motor fluctuations substantially impair daily functioning, treatment reliability, and quality of life in patients with PD.[11,12]

In the present study, patients with *H. pylori* infection had higher MDS-UPDRS Part III scores at baseline in both OFF and ON medication states compared to those who tested negative. This pattern is suggestive of a higher level of motor involvement in the infected group at the time of assessment. The difference was more marked in the OFF state, with a mean score of 60.8 ± 2.5 in the *H. pylori*-positive group and 30.7 ± 3.6 in the negative group. Such a wide separation between groups suggests that *H. pylori* infection may contribute to motor worsening, especially during periods of reduced levodopa effect. The results reported here are consistent with those of Tan *et al*., who reported that *H. pylori* infection was associated with greater severity of Parkinson's disease.[13] Successful H. pylori eradication has been associated with reduced daily OFF time and increased ON time in patients with advanced PD and motor fluctuations.[14] Recent biomarker-based approaches have also highlighted the potential value of objective molecular assessment in understanding and evaluating Parkinson's disease.[15] Pierantozzi et al. further demonstrated that H. pylori eradication could improve levodopa absorption in patients with PD and motor fluctuations.[16]

Nevertheless, published evidence on the association between *H. pylori* infection and motor impairment in PD remains inconsistent. In contrast to the present findings, a randomized placebo-controlled trial reported no significant improvement in motor, non-motor, or quality-of-life outcomes following *H. pylor*i eradication in patients with Parkinson's disease, suggesting that the clinical effect of eradication may vary across patient populations.[17] Such conflicting findings may reflect methodological differences, including variation in diagnostic tests used for *H. pylori*, differences in sample size, disease stage, levodopa regimen, regional strain virulence, dietary practices, gastrointestinal comorbidities, and prior exposure to acid-suppressive or antimicrobial therapy. Therefore, while the present findings support a clinically relevant association, they should be interpreted in the context of these potential sources of variability.

In addition, our study showed that eradication of HP infection resulted in a statistically significant improvement in UPDRS scores. The decrease in OFF-state scores (60.8 ± 2.5–54.4 ± 4.7) and ON-state scores (42.5 ± 4.7–40.3 ± 1.8) support the hypothesis that the gastrointestinal environment is pivotal in optimizing dopaminergic therapy. These observations are consistent with previous evidence indicating that *H. pylori* infection can alter levodopa pharmacokinetics and that eradication may improve levodopa absorption and therapeutic response.[18]

A possible mechanism is the direct metabolism of levodopa by HP which may reduce the systemic availability of the drug.[17,18] In addition, HP-induced chronic gastritis causes delayed gastric emptying and alterations in gastric pH, both of which affect levodopa dissolution and subsequent delivery to the site of absorption in the small intestine.[18,19] Gastrointestinal dysbiosis may also influence motor response,

as Gabrielli et al. reported a high prevalence of small intestinal bacterial overgrowth in patients with PD.[20] As also pointed out by Fasano *et al.*[21], restoration of gastrointestinal physiology after appropriate treatment may result in more consistent levodopa bioavailability.

Our study showed significantly older age and later onset of PD in HP-positive patients. This was also consistent with trend in Dobbs *et al*. which suggested an age-related increased susceptibility to HP colonization.[20-22] Interestingly, lifestyle factors such as lower intake of fruits and vegetables and smoking were more common in HP-positive patients. These factors have been previously implicated in poor eradication success and could influence gut microbiota and drug metabolism,[23,24] although not statistically significant in our cohort.

Our study is clinically relevant evidence of the impact of HP on the motor fluctuations and benefits of eradication, but it has some limitations to be acknowledged. Single-center design and relative small sample size may limit generalizability. However, the targeted inclusion of patients with motor fluctuations increases the internal validity.

Clinical diagnosis of *H. pylori* eradication was based on the resolution of gastrointestinal symptoms (dyspepsia, bloating, and early satiety) and motor function improvement at 6 weeks after treatment. Repeat endoscopy or stool antigen testing was not carried out due to resource constraints. Patients with both gastrointestinal symptom improvement and improvement in MDS-UPDRS-III score were considered as probable eradication. While this approach is practical, this is a limitation as microbiological confirmation was not performed.

Another limitation of the present study is the relatively short follow-up period after eradication therapy, which limits assessment of the long-term sustainability of motor improvement. Longer observation is required to determine whether the reduction in motor fluctuations persists over time. Nevertheless, the findings add support to the growing interest in the microbiota-gut-brain axis as a potential therapeutic target in PD. With growing attention on the role of intestinal microbial imbalance and gastrointestinal abnormalities in influencing PD progression and day-to-day symptom variation, screening for *H. pylori* infection and providing appropriate eradication therapy may represent a practical supportive approach in PD care. Further evidence should be generated through large, multicenter randomized trials that include objective confirmation of eradication, longer follow-up periods, and subgroup analysis to determine whether the observed motor benefits are sustained and which patients are most likely to benefit.

CONCLUSION

In this study, patients with PD showed a measurable improvement in MDS-UPDRS motor scores, after therapy for *H. pylori*, with the most marked benefit seen in early "OFF" episodes. The improvement may be related to a more reliable response to levodopa as indicated by longer ON duration, faster onset of drug action and fewer instances of early dose failure. These findings imply that gastrointestinal factors might be relevant to the assessment of motor complications in PD, especially in patients with fluctuating or inconsistent responses to medication. Thus, management strategies to improve gut function and levodopa absorption, including treatment of *H. pylori* infection, may offer useful additional benefit in selected patients.

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