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PRESCRIBING PRACTICES AND OUTCOMES OF ANTI-PARKINSONIAN MEDICATIONS IN INDIA: CURRENT STATUS AND FUTURE PROSPECTS

K. U. Janmita *, B. S. Spurthi, K. J. Sara Sandal and Shailesh Yadav

Department of Pharmacy Practice, Mallige College of Pharmacy, Bangalore - 560090, Karnataka, India.

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Correspondence to Author:
Dr. K.U. Janmita

Pharm D ,
Department of Pharmacy Practice,
Mallige College of Pharmacy,
Bangalore - 560090, Karnataka, India.

E-mail: kujapharmd24@gmail.com

ABSTRACT: Background: Managing Parkinson's disease (PD) requires a multimodal strategy, with pharmaceutical therapies being an essential component. This study's goal was to look into how antiparkinsonian drug prescriptions are given to PD patients at a tertiary care facility. **Methods:** Five hundred Parkinson's disease (PD) patients who visited the Department of Neurology at Mallige Hospital in Bengaluru, India, participated in an observational, cross-sectional study. Patients' medication histories were used to stratify them into three different groups: Group 1 (patients on medications at initial visit), Group 2 (patients who discontinued medications), and Group 3 (Drug-naïve patients). **Results:** The average age of PD onset was 51.5 ± 11.6 years. The patients were divided into three groups at the first visit: 76.4% (n=382) were on medications for PD (Group 1), 12.6% (n=63) had previously taken medications but discontinued (Group 2), and 11% (n=55) were drug-naïve (Group 3). Overall, levodopa was prescribed in 90.33%, trihexyphenidyl in 34.38%, in group 1, 48.7% were on monotherapy, with levodopa being the most commonly used agent (42.9%), followed by trihexyphenidyl. In group 2, levodopa monotherapy was also most common (65.07%), followed by trihexyphenidyl monotherapy (3.17%). **Conclusion:** This study highlights the prevalent use of levodopa and trihexyphenidyl in Parkinson's disease management, likely attributed to their accessibility, affordability, and tolerability. The findings underscore the need for tailored guidelines to optimize PD pharmacological management in the Indian context, considering factors such as medication costs, physician expertise, and potential side effects.

INTRODUCTION: Parkinson's disease is a multifaceted neurological disorder that has puzzled researchers for centuries. First described by James Parkinson in 1817, it is now recognized as the second most common neurodegenerative condition globally.

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Parkinson's affects a significant proportion of older adults, with prevalence rates ranging from 1-2% among individuals over 60. Interestingly, men are more likely to develop the disease than women, with a male-to-female ratio of 1.5:1.0. Overall, Parkinson's disease remains a complex and intriguing condition that warrants further research [1, 2, 3].

It is distinguished by the degeneration of nigrostriatal neurons and the formation of Lewy bodies, which contain alpha-synuclein. This neuronal loss leads to dopamine deficiency, resulting in lifelong disability [3, 4].

A complex interplay of environmental, lifestyle and genetic factors contributes to the progression of a debilitating neurodegenerative disorder. Motor symptoms manifest as resting tremors, bradykinesia, gait disturbances and cog-wheel rigidity, while non-motor symptoms encompass a range of neuropsychiatric and autonomic disorders.

These symptoms collectively contribute to a decline in quality of life, increased healthcare costs, limitations in daily activities and a growing need for care. The interaction between genetic predispositions – including mutations in genes such as Parkin/ PARK2 gene, Alpha-synuclein and Leucine rich repeat kinase-2 (LRRK2) / PARK8 gene and ATP13A2 gene – and environmental risk factors like pesticide exposure and lifestyle choices, plays a critical role in facilitating neuronal degeneration [3].

Multiple cellular processes converge to drive the pathogenesis of Parkinson's disease, with key features including α-synuclein misfolding, disrupted protein degradation pathways, including both lysosomal-mediated autophagy and the ubiquitin-proteasome system, that contribute to protein accumulation and toxicity along with mitochondrial dysfunction.

This complex biology underlies the disease's diverse motor and non-motor symptoms, which can be managed through targeted therapeutic strategies, including pharmacological interventions such as dopamine agonists (DA), levodopa (LD) along with other supportive medications, inclusng anticholinergics, MAO-B inhibitors, COMT inhibitors [5, 6, 7, 8].

MATERIALS AND METHODS: A cross-sectional, observational study was carried out on patients with PD attending the Department of Neurology at Mallige Hospital, Bengaluru, India. This study was approved by the Institutional Ethics Committee (approval number: MCP/RRB/010/22-23) prior to its commencement.

The study included patients diagnosed with Parkinson's disease during a 24-month period, spanning from 2022 to 2024. The diagnosis of PD was established based on Movement disorder society clinical diagnostic criteria for Parkinson’s disease.

A comprehensive review of patient records yielded demographic, clinical, and medication data, including age, age at onset, gender, Hoehn and Yahr staging. Additionally, a detailed medication history was compiled, documenting the dosage and duration of each medication.

Patient Selection and Eligibility: A total of 715 patients with a diagnosis of Parkinson's disease (PD) were initially identified. However, 110 patients did not meet the eligibility criteria, leaving 605 patients who were eligible for the study.

Exclusion Criteria: The study excluded 105 patients based on the following criteria:

- Atypical or secondary parkinsonism.
- Neurosurgery for PD.
- Significant cognitive impairment or dementia.
- History of psychosis or hallucinations.
- Incomplete or missing medical records.

Inclusion Criteria:

- A cohort of 500 patients were eligible for the study.
- Patients with a confirmed and documented diagnosis of Parkinson's disease (PD).
- Prescribed anti-parkinsonism medication(s) for at least 6 months.
- Individuals aged 18 or older, of both male and female genders.
- Able to provide informed consent.

Study Groups: The eligible patients (n=500) were stratified into three distinct groups:

1. Group 1 (n= 382), Patients on medication at baseline;
2. Group 2 (n= 63), Patients who had taken medication in the past but were no longer on treatment;
3. Group 3 (n=55), comprising drug-naive patients who had never received any medications for PD (**Fig. 1**).

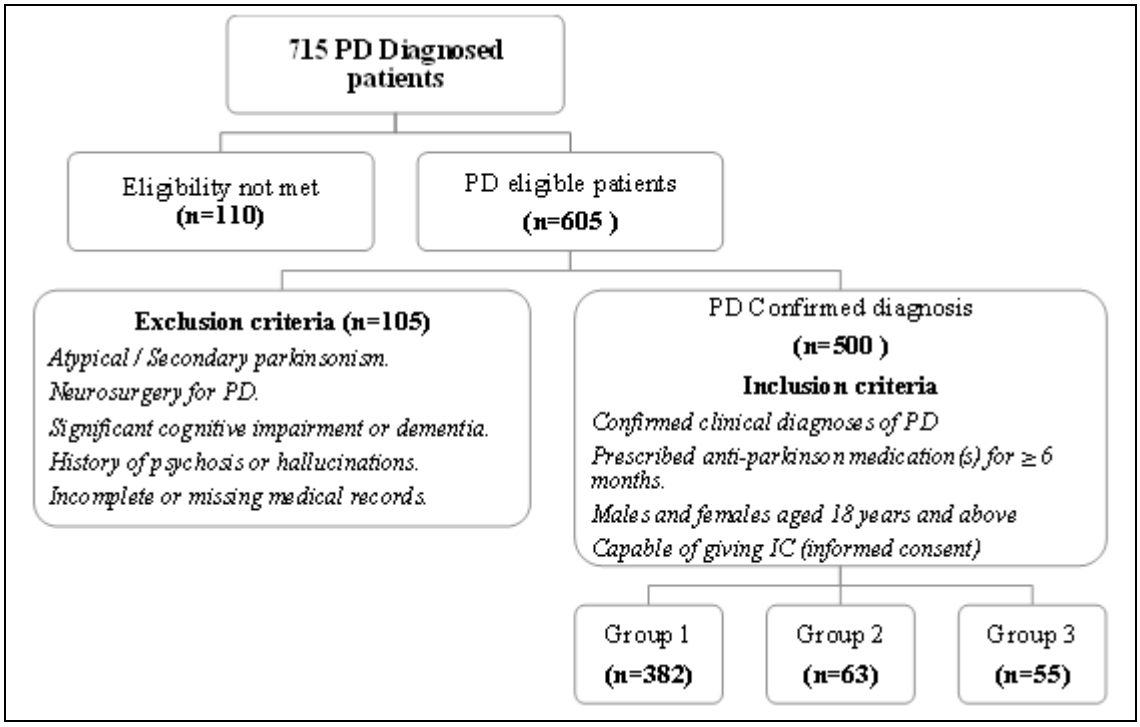

FIG. 1: PATIENT SELECTION AND ELIGIBILITY FLOWCHART

Statistical Analysis: Statistical analysis was conducted using a one-way ANOVA test, followed by post-hoc Bonferroni analysis, to compare demographic and disease characteristics among the patient groups. A significance level of $p < 0.05$ was used. Additionally, the chi-square test was employed to calculate the mean Levodopa Equivalent Daily Dose (LEDD) according to Parkinson's disease subtype and presence of dyskinesia. The relationship between Total LEDD (T-LEDD) and Hoehn & Yahr (H&Y) staging was assessed using Pearson's correlation analysis.

The levodopa equivalent daily dosage (LEDD) was calculated for patients in Groups 1 and 2 using standardized formulae with conversion factors of ×1 for immediate-release levodopa, ×0.75 for controlled-release levodopa, and various factors for other dopaminergic medications, resulting in two measures: total LEDD (T-LEDD), which combined all dopaminergic medication doses, and LD-LEDD, [9] which only included immediate-release and controlled-release levodopa doses as mentioned in **Table 1.**

RESULTS:

General Characteristics of the Study Cohort: 500 patients were included in the study, comprising 381 men 76.2% and 119 women 23.8% **Fig. 2.** The mean age of the patients with Parkinson's disease (PD) was 55.46 ± 11.2 years, with a mean age at onset of motor symptoms of 51.5 ± 11.6 years. The mean age at onset of motor symptoms varied slightly across the three groups: 52.8 ± 10.9 years in Group 1, 51.2 ± 12.3 years in Group 2, and 50.9 ± 11.9 years in Group 3. However, these differences were not statistically significant. A significant male predominance was observed in all three groups, with a marked difference between Group 1 and Group 2 ($p < 0.001$) and between Group 2 and Group 3 ($p < 0.01$). However, the Hoehn and Yahr (H&Y) stage distribution was similar across the three groups, with no significant differences observed **Table 1.**

TABLE 1: GENERAL CHARACTERISTICS OF THE STUDY COHORT

	Whole sample	Group1	Group2	Group3	Comparison		
Characteristic	**(*N*=500)**	**(*n*=382)**	**(*n*=63)**	**(*n*=55)**	**1vs.2***	**2vs.3***	**3vs.1***
Age (in years)	55.46±11.2	55.1±11	54.40±12.90	53.60 ±11.90	1.00	1.00	0.75
Age a ton set, years	51.5±11.6	52.8±10.9	51.20 ±12.30	50.90±11.90	1.00	1.00	1.0
Women, *n*(%)	119(23.8%)	83 (21.7%)	19(30.2%)	17(30.9%)	0.09	0.57	0.01
Men, *n* ***(%)***	381 (76.2%)	299 (78.2%)	44 (69.8%)	38(69.09%)	0.08	0.01	0.45
H&Ystage, *n*±*SD*	02.2±0.79	02.3±0.8	02.2±0.8	2.1±0.7	1.0	1.0	0.4

*Total LEDD, *n*±*SD*	451.33± 297.5	481.5±311.2	278.5±202.8	–	<0.001	–	–
LEDD, *n*±*SD*	374.31±330.27	376.20±355.3	371.6±106.1	–	<0.001	–	–
History of dyskinesia, *n*(%)	*81*(16.2%)	75(19.63%)	6 (9.52%)	–	0.02	–	–

***STANDARD CONVERSION FACTORS FOR CALCULATING TOTAL LEDD IN PD MANAGEMENT [9]**

Drug Class	Drug (D)	Conversion Factor/Ratio
L-DOPA	IR	DD × 1
	CR	DD × 0.75
	ER	DD × 0.5
COMT Inhibitors	Entacapone	LD × 0.33
	Tolcapone	LD × 0.5
MAO-B Inhibitors	Oral Selegiline	DD × 10
	Sublingual Selegiline	DD ×80
	Rasagiline	DD × 100
Non-ergot derived dopamine receptor agonists	Pramipexole (ER/IR)	DD × 100
	Ropinirole (ER/IR)	DD × 20
	Rotigotine	DD × 30
Others	Amantadine	DD × 1

Note: DD: daily dose; LD: levodopa dose; L-DOPA: levodopa; COMTi: catechol-O-methyl transferase inhibitor, MAO–Bi: monoamine oxidase B inhibitor; IR: Intermediate release; ER: Extended Release; CR: Control Release;

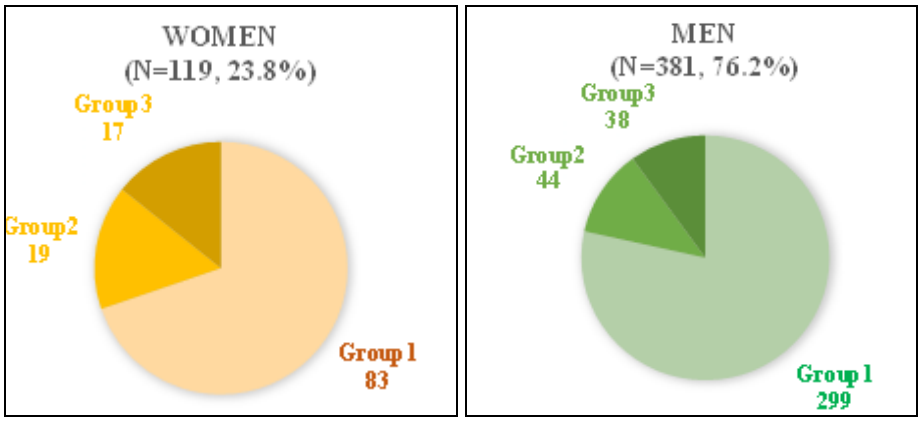

FIG. 2: GENDER DISTRIBUTION ACROSS TREATMENT GROUPS

Baseline Medication Pattern: The patients were divided into three groups at the first visit: 76.4% (n=382) were on medications for PD (Group 1), 12.6% (n=63) had previously taken medications but discontinued (Group 2), and 11% (n=55) were drug-naïve (Group 3).

Levodopa (LD) was the most frequently prescribed medication in both Group 1 (90.83%) and Group 2 (87.3%), used either as monotherapy or in combination with other medications **Table 3.**

The treatment regimens employed in Group 1 consisted of monotherapy (48.7%), dual therapy (35.07%), and triple or polytherapy (16.2%). Notably, levodopa (LD) monotherapy was the most prevalent treatment approach, accounting for 42.9% of patients, followed by THP monotherapy (2.6%). Among patients receiving polytherapy, 51.3% were administered multiple medications, with the combination of LD and THP being the most frequently employed regimen (21.46%). In contrast, Group 2 patients predominantly received LD monotherapy (65.07%), followed by THP monotherapy (3.17%) and the combination of LD and THP (12.7%) **Table 2.**

Notably, polypharmacy with three or more antiparkinsonian medications was not observed in this group. A detailed analysis of prescription patterns revealed that THP was the second most frequently prescribed medication, following levodopa LD. A statistically significant difference was observed in the prevalence of dyskinesia, with Group 1 exhibiting a higher incidence (19.3%) compared to Group 2 (9.52%), as confirmed by a p-value of 0.02 **Fig. 3.**

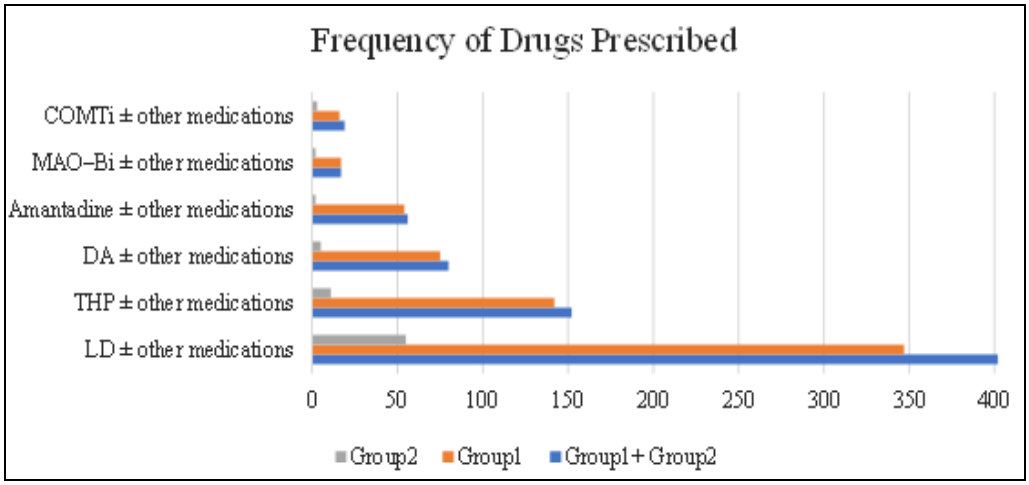

FIG. 3: FREQUENCY DISTRIBUTION OF ANTIPARKINSONIAN MEDICATIONS

TABLE 2: PROFILE OF THE STUDY COHORT'S PHARMACOLOGY

Medications	Group 1+2 (*n*=445)	Group1 (*n*=382)	Group2 (*n*=63)
Monotherapy	234(52.6 %)	186(48.7%)	48(76.2%)
LD	205(46.06%)	164(42.9%)	41 (65.07%)
THP	12(2.7%)	10(2.6%)	2 (3.17%)
DAs	8(1.8%)	6(1.57%)	2 (3.17%)
Amantadine	4(0.9%)	4(1.04%)	0
COMTi	3 (0.7%)	2 (0.5%)	1 (1.58%)
MAO–Bi	2(0.4%)	0	2 (3.17%)
Dual therapy	149 (33.48%)	134 (35.07%)	15 (23.8%)
LD+THP	90(20.2%)	82(21.46%)	8(12.7%)
LD+DA	24(5.4%)	22(5.75%)	2 (3.17%)
LD+ Amantadine	16(3.6%)	14 (3.66%)	2 (3.17%)
LD+COMTi	6 (1.3%)	4(1.04%)	2(3.17%)
LD+MAO–Bi	4 (0.9%)	4 (1.04%)	0.0
MAO–Bi + DA	2.0(0.4%)	2.0(0.52%)	0.0
DA+THP	2.0(0.4%)	1.0(0.26%)	1 (1.58%)
DA+ Amantadine	2.0(0.4%)	2.0(0.52%)	0.0
MAO–Bi +Amantadine	1.0 (0.2%)	1.0(0.26%)	0.0
MAO–Bi +THP	1.0 (0.2%)	1.0(0.26%)	0.0
THP+ Amantadine	1.0 (0.2%)	1.0(0.26%)	0.00
TripleorPolytherapy	62(13.9%)	62(16.2%)	0
LD+DA+THP	18(4.04%)	18(4.7%)	0.0
LD+THP+Amantadine	10(2.24%)	10(2.6%)	0.0
LD+DA+THP+Amantadine	8(1.8%)	8(2.09%)	0.0
LD+DA+Amantadine	6(1.3%)	6(1.57%)	0.0
DA+THP+Amantadine	4(0.9%)	4(1.04%)	0.0
COMTi+LD+MAO–Bi	2.0(0.4%)	2.0 (0.52%)	0.0
COMTi+LD+Amantadine	2.0(0.4%)	2.0 (0.52%)	0.0
COMTi+LD+DA	2.0(0.4%)	2.0 (0.52%)	0.0
COMTi+LD+THP	2.0(0.4%)	2.0 (0.52%)	0.0
MAO–Bi+ LD+THP	2.0(0.4%)	2.0 (0.52%)	0.0
MAO–Bi+ LD+DA	2.0(0.4%)	2.0(0.52%)	0.0
MAO–Bi+ DA+THP	1.0 (0.2%)	1.0 (0.26%)	0.0
MAO–Bi+ LD+THP+COMTi	1.0 (0.2%)	1.0 (0.26%)	0.0
MAO–Bi+ LD+DA+Amantadine	1.0 (0.2%)	1.0 (0.26%)	0.0
LD+THP+Amantadine +COMTi	1.0 (0.2%)	1.0 (0.26%)	0.0

Note: LD: levodopa; THP: trihexyphenidyl; COMTi: catechol-O-methyl transferase inhibitor; DA: dopamine agonist; MAO–Bi: monoamine oxidase B inhibitor;

Analysis of LEDD Doses: The mean daily T-LEDD was found to be 451.33 ± 297.5 mg for the overall population, with a significant disparity observed between Group 1 (481.5 ± 311.2 mg) and

Group 2 (278.5 ± 202.8 mg), yielding a p-value of ≤ 0.001. Additionally, the mean LD-LEDD for the entire cohort was 374.31 ± 330.27 mg, with mean values of 376.2 ± 355.3 mg and 371.3 ± 106.1 mg reported for Group 1 and Group 2, respectively. A comparative analysis was conducted to investigate the difference in T-LEDD) between patients with and without a history of dyskinesia in Group 1 (n=382). The results showed that patients with a history of dyskinesia (n = 75) had a significantly higher T-LEDD (564.25 ± 327.67 mg/day) compared to those without a history of dyskinesia (n = 307; 445.34 ± 280.56 mg/day) **Table 1.** A statistically significant difference in T-LEDD values was observed between Group 1 and Group 2 (p ≤ 0.001). These findings suggest that patients with a history of dyskinesia require higher doses of levodopa equivalent medications to manage their symptoms, which may be attributed to the development of motor complications. The results of this study highlight the importance of tailoring treatment approaches to individual patient needs, taking into account their history of dyskinesia and other clinical factors. Furthermore, the findings underscore the need for careful dose adjustment and monitoring of patients with dyskinesia to minimize the risk of adverse effects and optimize treatment outcomes.

TABLE 3: FREQUENCY DISTRIBUTION OF ANTIPARKINSONIAN MEDICATIONS

Medications	Group 1+2 (*n*=445)	Group 1 (*n*=382)	Group 2 (*n*=63)
LD±othermedications	402(90.33%)	347(90.83%)	55(87.3%)
THP±othermedications	152(34.38%)	142(37.17%)	11(17.4%)
DA±othermedications	80(17.97%)	75(19.36%)	5(7.93%)
Amantadine±othermedications	56(12.58%)	54(14.13%)	2(3.17%)
MAO–Bi±othermedications	17(3.82%)	17(4.45%)	2(3.17%)
COMTi±othermedications	19(4.26%)	16(4.18%)	3(4.76%)

Note: LD: levodopa; THP: trihexyphenidyl; DA: dopamine agonist; MAO–Bi: monoamine oxidase B inhibitor; COMTi: catechol-O-methyl transferase inhibitor

Clinical features of Parkinson's disease: Pre and Post Treatment Assessment: A comparative analysis of the three cohorts revealed disparate frequencies of both motor and non-motor symptoms were evident in the patient population prior to the initiation of treatment. Group 1 exhibited Resting tremor in 96.85% of patients, Bradykinesia in 95.54%, and Rigidity in 95.54%, concomitant with neuropsychiatric disorders in 57.6% and Autonomic disturbances in 48.4%. In Group 2, the corresponding frequencies were 88.88% for Resting tremor, 78.77% for Bradykinesia, and 73.01% for Rigidity, alongside neuropsychiatric disorders in 63.5% and Autonomic disturbances in 50.8%. Group 3 presented a distinct symptomatological profile, marked by resting tremor in 78.18% of patients, Bradykinesia in 81.81%, neuropsychiatric disorders in 45.45%, and Autonomic disturbances in 49.09%. The post-treatment assessment revealed substantial amelioration of both motor and non-motor symptoms, indicating a positive treatment response. Motor symptoms reduced by 40.57% (resting tremor), 32.72% (bradykinesia), and 39.26% (rigidity) in Group 1, and by 21.58%, 16.87%, and 17.49% in Group 2. Non-motor symptoms reduced by 15.68% (autonomic disturbances) and 16% (neuropsychiatric disorders) in Group 1, and by 8% and 11.2% in Group 2. However, Group 3 showed worsening of non-motor symptoms (27.27% increase in autonomic disturbances, 23.64% in neuropsychiatric disorders) and motor symptoms **Fig. 4.** This highlights the importance of timely and effective intervention. The study demonstrates the treatment's therapeutic potential in mitigating motor and non-motor symptoms in PD patients, emphasizing personalized approaches and regular monitoring **Table 4.**

TABLE 4: CLINICAL FEATURES OF PARKINSON'S DISEASE: PRE- AND POST-TREATMENT ASSESSMENT

Clinical Features	Before Treatment			After Treatment		
	Group 1 (n=382)	Group 2 (n=63)	Group 3 (n=55)	Group 1 (n=382)	Group 2 (n=63)	Group 3 (n=55)
Motor symptoms						
Resting tremor	370(96.85%)	56(88.88%)	43(78.18%)	215(56.28%)	44(69.8%)	50(90.90%)
Bradykinesia	36(95.54%)	49(78.77%)	45(81.81%)	240(62.82%)	39(61.9%)	48(87.27%)

Rigidity	365(95.54%)	46(73.01%)	51(92.72%)	250(56.28%)	35(55.55%)	53(96.36%)
Gait disturbances/Postural instability	219 (57.3%)	35(55.55%)	37(63.2+7%)	170(44.50%)	29(46.03%)	37(67.27%)
Micrographia	240(62.8%)	29(46.03%)	25(45.45%)	170(45.45%)	20(31.7%)	30(54.45%)
Masked facies (Hypomimia)	340(89.0%)	33(52.38%)	30(54.54%)	211(55.23%)	27(42.85%)	41(74.54%)
Dysphagia	80(20.9%)	19(30.15%)	12(81.81%)	55(14.39%)	15(23.8%)	20(36.36%)
Decreased arm swinging while walking	375(98.16%)	39(61.9%)	24(43.63%)	211(45.45%)	33(52.3%)	35(63.63%)
Frequent falls	165(43.19%)	20(31.7%)	25(45.45%)	95(24.8%)	15(23.8%)	30(54.54%)
Non-Motor disorders						
Autonomic disturbances (orthostatic hypotension, Sialorrhea, Constipation, Urinary incontinence)	185(48.4%)	32(50.8%)	27(49.09%)	125(32.72%)	27(42.8%)	42(76.36%)
Neuropsychiatric disorders (Depression, Anxiety, Agitation, Cognitive impairment/Dementia)	220(57.6%)	40(63.5%)	25(45.45%)	159(41.6%)	33(52.3%)	38(69.09%)

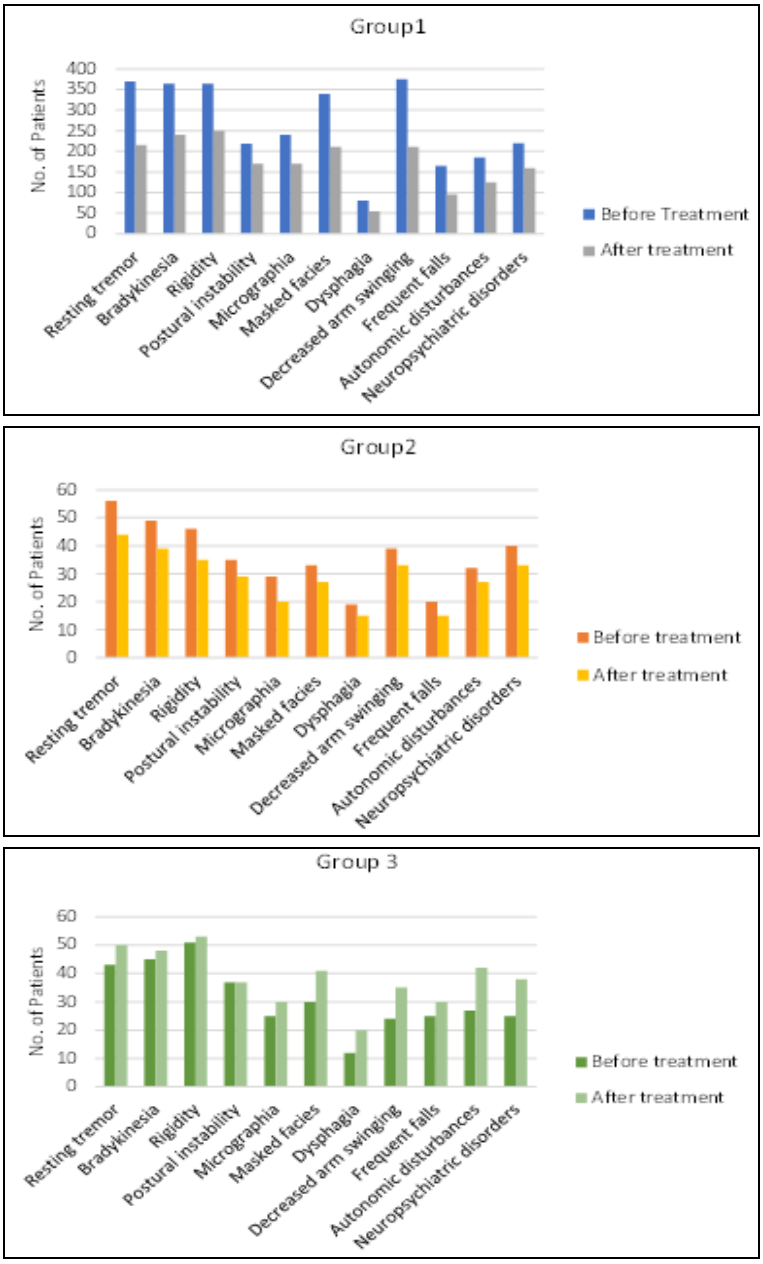

FIG. 4: CLINICAL FEATURES OF PARKINSON'S DISEASE: PRE- AND POST-TREATMENT ASSESSMENT FOR DIFFERENT GROUPS

ADR Profile: The adverse drug reaction (ADR) profile revealed that levodopa was associated with dyskinesia (19.63%), anorexia (3.45%), and hallucination (1.50%), while anticholinergic medications were linked to dry mouth (4.45%), urinary retention (3.90%), sedation (8.30%), and constipation (4.90%) in Group 1, and similar ADRs were observed in Group 2, including dyskinesia (9.52%), anorexia (11.11%), hallucination (3.17%), dry mouth (6.30%), urinary retention (9.50%), sedation (6.30%), and constipation (7.90%), highlighting the distinct ADR profiles of these medications **Fig. 5.**

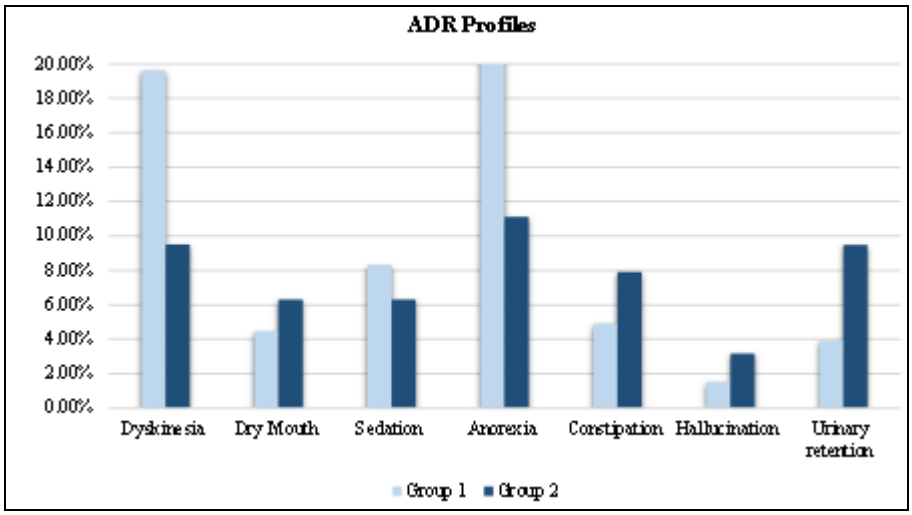

FIG. 5: ADR PROFILES LEVODOPA AND ANTICHOLINERGIC MEDICATIONS

DISCUSSION: A deeper understanding of anti-parkinson drugs prescribing patterns is vital to address the multifaceted challenges posed by this debilitating neurodegenerative disorder. This study was undertaken to evaluate drug prescribing pattern, to analyse the correlation between mean drug dose per day with the symptomatic prognosis of disease along with associated ADRs in a tertiary care referral hospital. Our study contributes to this effort by examining the prescribing trends among 500 PD patients. A male predominance of 3.2:1 ratio, likely due to the protective effects of estrogen, which regulates dopamine levels. Gene expression studies revealed sex-specific differences in dopamine neurons, with females showing upregulation of genes involved in neuronal health and males showing upregulation of genes linked to PD, such as PINK1 and alpha-synuclein [10]. Approximately 23.60% patients, comprising of groups 2 and group 3, denied taking any medications at their initial OPD (out-patient department) visit, which can be attributed to various reasons:

- Medication related (Adverse effects, Lack of efficacy, Motor fluctuations, Dyskinesias, Cognitive decline, Psychiatric symptoms, Medication interactions)
- Patient - Related factors (Cost/accessibility issues, Patient preference, Disease progression, Poor medication adherence, Alternative therapies)

The most frequently prescribed medications were either LD as monotherapy (46.06%) or LD combined with THP (20.2%) and DA (5.4%). Our finding mirrors that of an American study by Orayj K and Lane E, which reported a decline in non-ergot DA prescriptions from 33.4% in 2008 to 27.9% in 2011, following the addition of warnings about impulse control disorders, including pathological gambling and hypersexuality, to the pramipexole profile [6].

Similarly, in India, the preference for LD and THP combinations over DAs may be due to factors including higher DA costs, physician inexperience, and concerns about DA side effects such as gastrointestinal issues, compulsive behaviour and hallucinations. In our study, THP was the second most frequently prescribed medication, used alone or in combination in 34.38% of cases, following LD which was prescribed alone or in combination in 90.33% of cases. Ideally, THP should be avoided in the elderly due to its anticholinergic effects,

which can lead to dry mouth, constipation, confusion, cognitive impairment, and urinary retention. However, in our study, THP was well-tolerated, possibly attributed to the younger average age at onset (55.46±11.20 years), compared to PD patients worldwide, where the average age at onset is typically higher (≥60.0 years) [6, 11]. Additionally, the high prevalence of tremor-predominant PD (93.8%) in our cohort may have contributed to the frequent use of THP.

MAO-B inhibitors, including rasagiline and selegiline, form a fundamental part of early Parkinson's disease management, largely owing to their neuroprotective effects [12]. Interestingly, our study revealed an underrepresentation of MAO-Bi, with a mere 3.82% of early PD patients receiving these medications, and selegiline being the more commonly prescribed option. Both Rasagiline and Selegiline are considered equally effective in early stages of PD, given their similar selective and irreversible mechanisms. However, they differ in their metabolites, with selegiline producing amphetamine derivatives and rasagiline producing aminoindane, which has neuroprotective properties. Despite this, selegiline is often preferred by prescribers due to its better tolerability, antidepressant effects, and improved symptomatic relief, which can delay the need for dopaminergic treatment[13].Safinamide, a novel oral MAO-B inhibitor approved in 2017, has shown efficacy when combined with DA for early-stage PD patients and in preventing LD-induced "on-off" phenomena. Safinamide stands out from traditional MAO-B inhibitors due to its unique pharmacological properties, including modulation of ion channels (calcium and sodium channels) and inhibition of release of glutamate, which may contribute to its neuroprotective effects and make it a valuable treatment option for PD [14].

The COMT inhibitors (COMTi) prescribing rates were the lowest among antiparkinsonian medications, at 4.26%. Specifically, tolcapone monotherapy had a notably low prescription rate of 1.3% in a 1997-1998 Italian study, likely as a result of the FDA's safety warning concerning to its risk of causing liver toxicity [15]. Despite being more potent and longer-acting than entacapone at similar doses, tolcapone's use as adjunctive therapy for levodopa-induced wear-off effects has been limited due to its hepatotoxicity and severe diarrhoea, side effects that are not associated with entacapone. According to the newer trials demonstrated on PD patients with BIPARK 1 and 2, Opicapone, a newer third-generation COMT inhibitor, was effective in reducing motor fluctuations in PD patients taking levodopa. Opicapone (50mg/day) significantly improved ON-time and reduced OFF-time, when compared to placebo and entacapone with sustained benefits over one year, and was well-tolerated across various patient populations, with positive clinical impressions reported by patients and clinicians [16, 17].

At study initiation, most patients showed classic Parkinson's disease symptoms, including resting tremors, decreased arm swing, bradykinesia, and rigidity, which were relatively mild compared in post-therapy **Table 4.** Following treatment, which lasted 22-24 months, most patients reported subjective improvements in symptoms. Specifically, significant improvements were observed in motor symptoms, including decreased arm swing (75.05%), resting tremors (72.3%), masked face (59.3%), bradykinesia (58.4%), rigidity (54.1%), and micrographia (33.4%). Non-motor symptoms also showed improvement in 57.07% of patients. Group 3 patients, who declined therapy, experienced a significant worsening of symptoms. This led to an increase in motor symptoms, including masked facies and decreased arm swinging while walking (20%), dysphagia (14.5%), resting tremor (12.2%), and bradykinesia (5.45%). Additionally, non-motor symptoms worsened, with 27.2% experiencing autonomic issues and 23.6% experiencing neuropsychiatric problems.

The marked difference in outcomes between treated and untreated patients (Group 3) highlights the vital importance of therapy in slowing or halting Parkinson's disease progression. Prompt treatment initiation is crucial to maximize benefits. Untreated, the condition can cause profound impairment, loss of autonomy, reduced quality of life, complicated by falls, cognitive decline, psychiatric issues, speech and swallowing problems, malnutrition, and shortened life expectancy, imposing a substantial burden on patients, caregivers and healthcare systems.

The adverse drug reaction (ADR) profile of levodopa and anticholinergic medications can be attributed to their distinct mechanisms of action. Levodopa's conversion to dopamine triggers pulsatile receptor stimulation, leading to abnormal motor responses, including dyskinesia. Reducing levodopa doses can alleviate dyskinesias, but may exacerbate parkinsonian symptoms, necessitating more frequent dosing or adjunctive therapies like amantadine. Consistent with this, our study found levodopa-induced dyskinesia to be the most common adverse drug reaction, managed by dose reduction, increased dosing frequency, or addition of sustained-release levodopa or amantadine (12.58%) [18]. Additionally, levodopa's effects on serotonin and other neurotransmitter systems may contribute to anorexia and hallucination. In contrast, anticholinergic medications' blockade of muscarinic acetylcholine receptors regulates salivation, bladder function, and gut motility, resulting in dry mouth, urinary retention, and constipation. Furthermore, the sedation associated with anticholinergic medications may be related to their effects on the brain's cholinergic systems, which regulate arousal and alertness.

CONCLUSION: This observational study offers a detailed understanding of the prescribing patterns of anti-parkinsonian medications in India, highlighting the need for optimized treatment strategies that balance efficacy, safety, and affordability. The findings show that the predominant use of levodopa and trihexyphenidyl is attributed to their accessibility, affordability, and tolerability. The importance of revising current treatment paradigms to incorporate emerging therapies, including MAO-Bi (e.g., rasagiline and selegiline), DA (e.g., pramipexole and ropinirole) and COMT inhibitors (e.g., tolcapone and entacapone), is emphasized. The underutilization of Safinamide, a next-generation MAO-B inhibitor offering neuroprotection, necessitates increased awareness and adoption in clinical practice. Findings highlight the crucial role of healthcare providers in delivering timely treatment and patient-centered care, informing a multidisciplinary approach to Parkinson's disease management that improves outcomes and accessibility.

Limitations: The study's generalizability is potentially compromised by the sample size (n=500), which may not be sufficiently representative of the broader Parkinson's disease population. The single-center design is vulnerable to various biases, including hospital-related bias (Berksonian bias), which can lead to an over representation of more severe or complex cases. Moreover, the disparate distribution of patients across the three groups may introduce unevenness in the data, potentially impacting the validity of the findings. Due to its cross-sectional nature, this study cannot establish causality, and the observational design limits the ability to infer cause-and-effect relationships. Furthermore, reliance on patient-reported medication history may introduce recall bias, and unadjusted confounding variables may compromise internal validity. Finally, the use of levodopa equivalent daily dose (LEDD) calculations may not fully capture the complexities of treatment regimens, introducing potential sources of bias and affecting the precision of the results.

Future Perspectives: Future studies should prioritize addressing the limitations of this research, including the need for larger, multicentre trials to enhance generalizability and reduce bias. Longitudinal designs would enable the establishment of cause-and-effect relationships, while adjusting for confounding variables would strengthen internal validity. Furthermore, incorporating objective measures of medication adherence and treatment outcomes would reduce reliance on patient-reported data. Investigating the influence of environmental and genetic factors on treatment response and prognosis of disease, would provide valuable insights into personalized medicine approaches. Additionally, exploring the potential benefits of novel therapeutic agents, such as safinamide, and optimizing treatment regimens to minimize adverse effects would be essential for improving patient outcomes. This investigation serves as a springboard for future research endeavours targeting the development of more effective PD management strategies and improved quality of life.

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