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Effect of Dopaminergic Drugs on Frontal Lobe Functioning and Impulse Control Disorder in Parkinson's Disease Patients

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ABSTRACT

Parkinson's disease (PD) is a neurodegenerative disorder characterized by motor and non-motor symptoms. Dopamine therapies, particularly dopamine agonists, are linked to Impulse Control Disorders (ICDs) that affect the quality of life. This study evaluates ICD prevalence in PD patients on dopamine therapy and examines dopaminergic drugs' effects on frontal lobe functioning. A six-month, prospective observational study was conducted at Magna Neurology Clinic, involving 120 PD patients (aged 19-75 years). Assessments included the UPDRS, Modified Hoehn and Yahr Staging, Schwab and England ADL Scale, PDQ-39, and QUIP-RS. Cognitive tests, such as the Stroop and Trail Making Tests, were also performed. Data analysis used GraphPad software with descriptive statistics and Pearson's correlation. The cohort was predominantly male (67%) with a mean age of 57.69±10.21 years. The disease onset was mostly between 1-5 years. A moderate positive correlation (0.3375, p=0.0002) was found between disease onset and daily dopaminergic dose. Depression (26.4%) was the most common symptom. UPDRS-III showed symptom improvement in the ON state, with rigidity and tremor being most prevalent. PDQ-39 highlighted impairments in Activities of Daily Living (33.81%) and Mobility (33.52%). Cognitive assessments showed a negative correlation between Stroop Reaction Time (SRT) and levodopa dosage, indicating improved attention. Trihexyphenidyl was associated with cognitive impairment. Dopaminergic therapies, particularly dopamine agonists, are linked to higher ICD prevalence. Levodopa improved cognitive attention, while trihexyphenidyl impaired it. Careful monitoring of dopaminergic therapy is necessary to balance symptom control, and further research is needed to explore strategies for mitigating ICD risks.

Keywords: Cognitive function, Dopaminergic therapy, Impulse Control Disorders (ICDs), Levodopa, Parkinson's disease

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INTRODUCTION

Long-term, progressive neurodegenerative disorder that leads to a gradual decline in both motor and non-motor function is the classic feature of Parkinson's disease (PD) [1,2]. Bradykinesia, tremors postural instability and rigidity are other major manifestations. The disease is defined by the progressive loss of dopaminergic neurons, primarily in substantia nigra region of the midbrain [3-5]. Impulse Control Disorder and Related Behaviours (ICD-RBs) encompass a group of complex behavioral disorders marked by an inability to resist urges or temptations, resulting in actions that may be harmful to oneself or others. These disorders can lead to significant distress and impairment in occupational or social functioning. These disorders have an impact on the lives of patients and are often un- recognized. Parkinson personality may be characterized by temperament and a decreased tendency to indulge in pleasant pleasures [6-8]. Patients undergoing treatment with dopamine agonists, such as Pramipexole or Ropinirole, have a higher risk of developing impulse control disorders compared to those receiving only dopamine precursors like levodopa [9,10]. Dopamine replacement therapy (DRT) can help reduce many of the debilitating motor symptoms associated with PD. These medications are designed to address motor

impairments resulting from nigrostriatal dopamine deficiency while also activating largely preserved mesocorticolimbic dopaminergic neurons [11]. DRT affects dopamine receptors in both the nigrostriatal and reward pathways, contributing to addictive behaviors and withdrawal symptoms. The primary approach to managing ICDs is reducing or discontinuing dopamine agonist therapy, but some patients struggle due to worsening motor symptoms or dopamine agonist withdrawal syndrome (DAWS), a severe non-motor withdrawal condition resembling that of cocaine and other stimulants. This issue, known as dopamine dysregulation syndrome, is mainly linked to potent, short-acting medications like levodopa. Although no specific drugs are approved for ICD treatment, the first-line strategy for severe cases is reducing the most recently adjusted Parkinson's medication. In some cases, lowering the L-dopa dose may also be necessary. Research shows that increasing L-dopa after dopamine agonist withdrawal to maintain motor function does not necessarily cause ICD recurrence, even at higher total daily L-dopa equivalents. Nevertheless, very few patients developed DDS. Some case reports suggest that switching from a short-acting DA (ropinirole, pramipexole) to a long- acting DA (piribedil) or treatment with a DA with less D3 receptor agonist action can be effective [12]. Drug and alcohol abuse can complicate the treatment of impulse control disorders and their pharmacological management, as interactions between substances and medications may lead to unintended consequences. Certain medications are not recommended for individuals with a history of substance abuse due to their habit-forming potential or risk of misuse. Therefore, a thorough drug screening is essential upon entering a treatment program to ensure the highest and safest level of care. Individuals dependent on psychoactive substances may benefit from a medical detox program before beginning treatment [13,14]. This study thus aims to examine the effect of dopaminergic drugs on frontal lobe functioning in patients diagnosed with Parkinson's disease and also to ascertain the prevalence of Impulse control disorder-related behaviors (ICD-RBs) in Parkinson's disease patients after receiving dopamine therapy.

MATERIAL AND METHODS

Study design

It is prospective observational study design in the outpatient department of Magna Neurology Clinic, Banjara Hills, Hyderabad over a six-month period from September 2021 to February 2022 following approval from the Institutional Ethics Committee of Anurag University. Study subjects who met the inclusion criteria were recruited following informed consent. Data was collected from 120 patients and their informants using standardized questionnaire tools, including the UPDRS, Schwab and England Activities of Daily Living Scale, Modified Hoehn and Yahr Staging, PDQ-39, and QUIP-RS. Additionally, cognitive assessments such as the Stroop test and Trail Making tests were administered. The data were analyzed to assess the impact of dopaminergic medications on frontal lobe function and the occurrence of ICD in individuals with PD.

Study population

Study subjects diagnosed with PD, of all genders, aged 19 to 75 years, attending the outpatient department of neurology, provided they were literate. Exclusion criteria comprised pregnant and lactating women, individuals with mental or physical disabilities, patients below 18 years of age, inpatients, and illiterate individuals.

Study method

A literature survey was conducted by reviewing various research papers related to the study. A data collection form was designed to gather the necessary information. In the outpatient department, patients diagnosed with PD were identified. Data was collected from them and their informants after obtaining informed consent. Standard questionnaire tools, including UPDRS I-IV, Modified Hoehn and Yahr Staging, Schwab and England Activities of Daily Living Scale, and QUIP-RS, were used to assess patient conditions, and their drug therapy details were recorded. Additionally, cognitive assessments, such as the Stroop Reaction Test and Trail Making Tests A&B, were performed on the patients.

Outcome Measurements

UPDRS (Unified Parkinson's Disease Rating Scale): A tool to track Parkinson's disease progression [15], comprising:

UPDRS-I: Mentation, Behavior, Mood (score 0-16).

UPDRS-II: Activities of Daily Living (score 0-52, ON/OFF states).

UPDRS-III: Motor examination (score 0-108).

UPDRS-IV: Therapy complications (score 0-23).

Hoehn and Yahr Staging: Stages 0-5 :Disease progression, No signs - wheelchair-bound.

Schwab and England ADL Scale: Measures independence, from 100% (completely independent) to 0% (vegetative state).

PDQ-39 (Parkinson's Disease Questionnaire-39): A 39-item survey assessing health status and quality of life across 8 dimensions ranging from mobility to body discomfort [16].
QUIP-RS (Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease) [17]**:**Assesses severity of impulse control disorders (ICDs) in 3 sections: gambling, hypersexuality, buying/eating behaviors, compulsive behaviors (punding, hobbyism, walkabout), and compulsive medication use.
Stroop Color-Word Test: A neuropsychological test measuring executive functioning, including selective attention, cognitive flexibility, inhibition, and processing speed, based on reaction times in congruent vs. incongruent conditions [18].
Trail Making Test (A&B): Measures cognitive functions like processing speed, mental flexibility, and visual-motor skills in which Part A infers connecting numbers 1-25 in ascending order and Part B inferring the connection of numbers and letters alternately in ascending order [19].
Data analysis: The study analysis was done using graph pad software. Descriptive statistics was used to determine the mean distribution. Pearson's correlation was used to find out the association between dopaminergic drugs with frontal lobe functioning and Impulse control disorders.

RESULTS
In a sample of 120 patients, subjects were predominantly of the age group between 55-65 years followed by age group between 46-55 years with 67% being males and 33% females. The study included 120 participants with a mean age of 57.69±10.21 years. Pearson's correlation analysis between age and the daily doses of dopaminergic drugs (LEDD) revealed a correlation coefficient of -0.09189, indicating a weak negative correlation. The association was not statistically significant (p = 0.3182). The 95% confidence interval ranged from -0.2667 to 0.08882. It was found from the study that only 16% of study subjects have consanguineous relationship whereas 84% were non-consanguineous. It was found that most of the patients had an onset period between 1-5 years followed by 6-10 years. The Pearson's correlation between disease onset and the daily doses of dopaminergic drugs (LEDD) was found to be 0.3375, indicating a moderate positive correlation. This correlation is statistically significant with a p-value of 0.0002 (2-tailed), and the 95% confidence interval ranges from 0.1684 to 0.4873 as in **Table 1.**

Table 1: Pearson's correlation between disease onset and daily doses of dopaminergic drugs (LEDD)

Disease onset vs. LEDD	Pearson's Correlation	Significance (2- tailed)	95% Confidence Interval	
			Lower	Upper
	0.3375	0.0002	0.1684	0.4873

Unified Parkinson's Disease Rating Scale (UPDRS)
Unified Parkinson's Disease Rating Scale to assess the severity of symptoms of Parkinson's disease. UPDRS-I is used to provide information about the subject's mentation, behavior and mood. The total mean score was found to be 2.91. Depression (26.4%, n=31) was found to be highest among other components in the study subjects followed by intellectual impairment (16.6%, n=20), thought disorder (15%, n=18) and motivation/initiative (14.7%, n=18). The mean distribution of each componentt of **UPDRS-I,** based on 120 participants presented, Intellectual impairment mean score of 0.66 (SD = 0.87, SE = 0.079), thought disorder had a mean score of 0.6 (SD = 1.02, SE = 0.093), depression had a mean score of 1.05 (SD = 0.97, SE = 0.088), and motivation/initiative had a mean score of 0.59 (SD = 0.99, SE = 0.089). The mean distribution for the total UPDRS-I score, based on 120 participants, obtained the mean score as 2.91, with a standard deviation of 2.78 and a standard error of 0.25. **UPDRS-II** is used to provide information on activities of daily living. The UPDRS-II scores were assessed in 120 individuals in both OFF and ON states. In the OFF state, the mean score was 16.82, with a standard deviation of 7.74 and a standard error of 0.7. In the ON state, the mean score decreased to 7.63, with a standard deviation of 5.45 and a standard error of 0.49. **Figure 1** illustrates mean scores of UPDRS-II scale in both ON and OFF condition. Scores in OFF condition were highest than in ON condition with handwriting having the highest score among other components.
The highest mean score in OFF condition was found to be 2.01 for handwriting followed by1.85 for dressing whereas in ON condition, the highest mean score was found to be 0.04 for dressing and 0.88 for handwriting. Handwriting and dressing were found to be mainly affected than other components in PD patients. **UPDRS-III** is used to examine the motor symptoms in PD. The total mean score was found to be 41.86 in OFF condition and 13.02 in ON condition. Rigidity was found to have the highest mean score 8.06 in OFF condition followed by 4.47 for tremor at rest whereas in ON condition, rigidity was found to highest with a mean score of 2.1 followed by finger taps with mean score of 1.44. In the OFF state, the mean UPDRS-III score was 41.87, with a standard deviation of 17.22 and a standard error of 1.57. In the ON

state, the mean score significantly decreased to 13.03, with a standard deviation of 7.57 and a standard error of 0.69. **Figure 2** depicts mean scores of UPDRS-III in both ON and OFF condition.

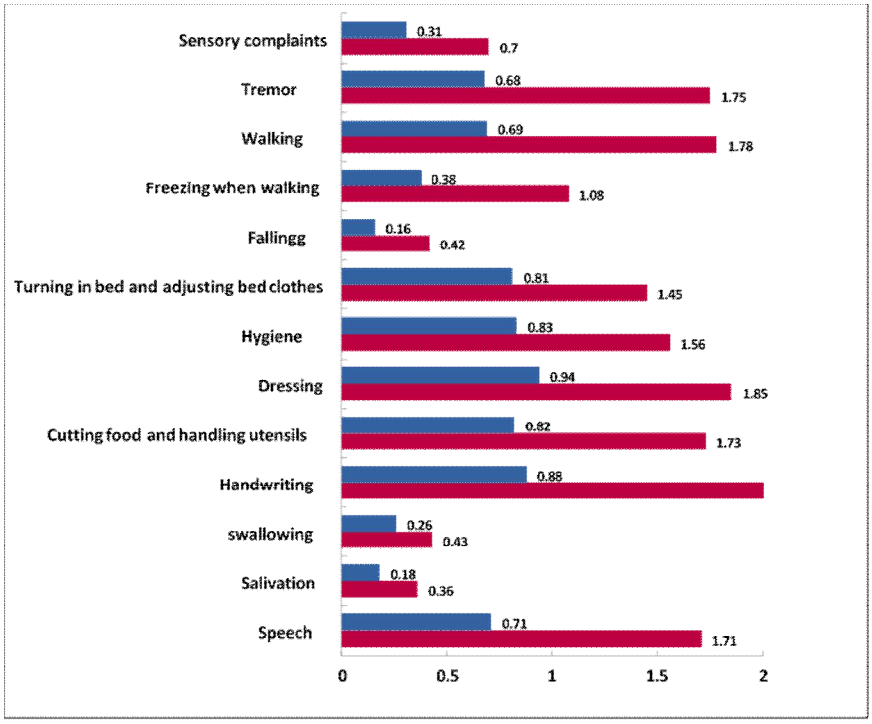

Figure 1: UPDRS-II-Activities of Daily Living

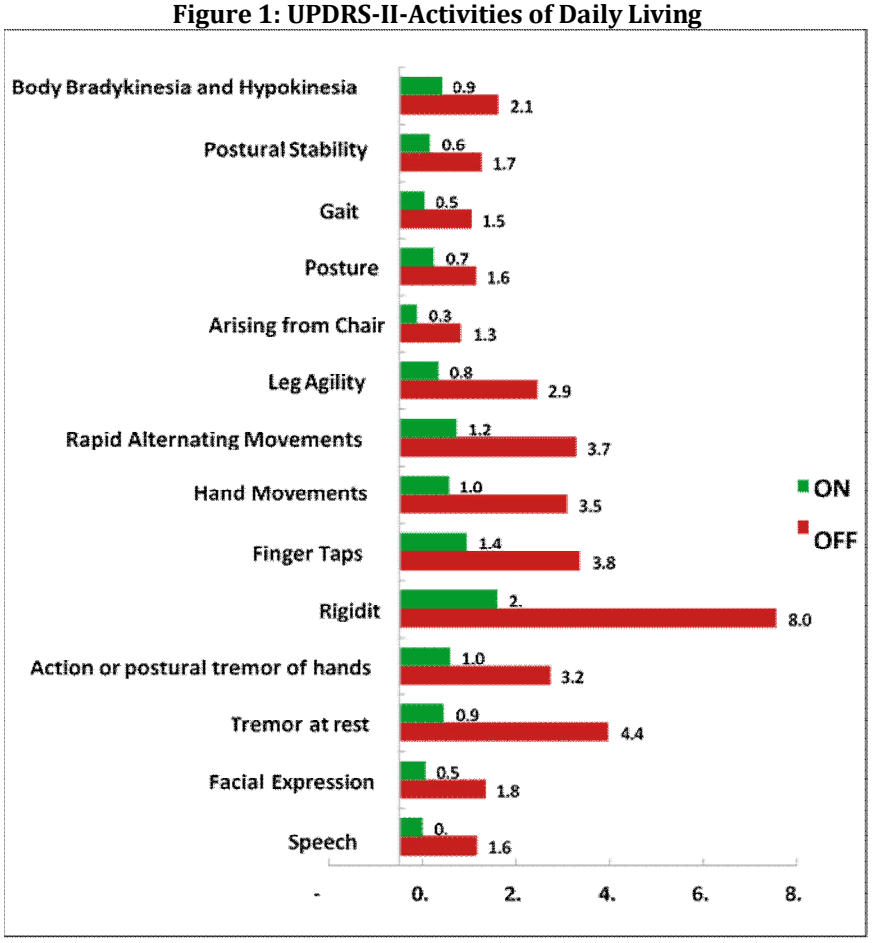

Figure 2 UPDRS-III: Motor Examination

Scores in the OFF condition were highest than in ON condition with rigidity having the highest score among other components. **UPDRS-IV** describes Complications of therapy of PD. The total mean score was found to be 1.48. Insomnia/ Hyper somnolence was found to be highest among the study subjects followed by dyskinesias, dystonia, anorexia/nausea/vomiting and symptomatic orthostasis with percentages as follows 38.3%, 35.8%, 25%, 17.5% and 16.6%. The mean distribution for each complication of UPDRS-IV is as follows: mean score for dyskinesia was 0.52, with a standard deviation of 0.82 and a standard error of 0.07. Dystonia had a mean score of 0.25, a standard deviation of 0.43, and a standard error of 0.03. The mean score for anorexia, nausea, and vomiting was 0.17, with a standard deviation of 0.56 and a standard error of 0.05. Insomnia or hypersomnolence had a mean score of 0.38, a standard deviation of 0.48, and a standard error of 0.04. Lastly, symptomatic orthostasis had a mean score of 0.16, with a standard deviation of 0.37 and a standard error of 0.03. This analysis done in 120 individuals observed a mean score of 1.5, with a standard deviation of 1.32 and a standard error of 0.12. Modified Hoehn and Yahr Staging scale is used to determine the degree of progression of PD. The total mean score was found to be 2.41. Among the study population, the highest percentage of subjects were found in Stage 1.5 (34%) followed by stage 3 (24%), stage 4(17%), stage 2 (11%), stage 2.5 (10%), stage 1 (4%).

Schwab and England Activities of Daily Living Scale

To assess the disability index (DI) of the study population, the Schwab and England Activities of Daily Living Scale was used. The findings revealed that 25% of the study subjects had a DI of 70%, followed by 20% with a DI of 60%, 13% with a DI of 90%, 11% with a DI of 50%, 6% with a DI of 40%, 3% with a DI of 30%, and 2% with a DI of 20%. The mean disability percentage is 66.5, the standard deviation is 0.16, and the standard error is 0.01. The **PDQ-39 scale** was used to assess the factors affecting the quality of life. The total mean score was found to be 38.8. The percentages of the study population affected by different factors of PDQ-39 were as follows: 33.81% for Activities of Daily Living, 33.52% for Mobility, 26.5% for Stigma, 25.62% for Communication, 23.36% for Emotional Well-Being, 19.86% for Body Discomfort, 12.76% for Cognition, and 1.73% for Social Support. Activities of Daily Living and Mobility were found to be the most significantly affected components, which could have a considerable impact on the quality of life. The sample analysis shows a mean score of 39.09, a standard deviation of 24.04, and a standard error of 2.19. Figure 8 depicts the percentage of different components of PDQ-39. **Figure 3** illustrates percentage of different drugs prescribed for Parkinson's Disease in the study population.

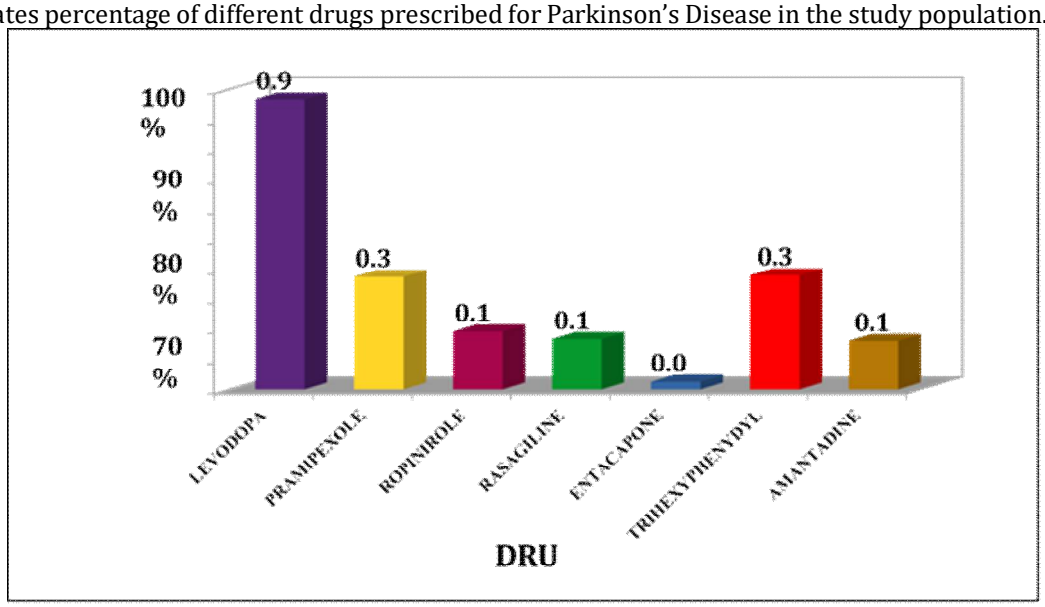

Figure 3: Pharmacotherapy of Parkinson's Disease

Most of the subjects were prescribed with Levodopa followed by Pramipexole and Trihexyphenydyl. For the different dopaminergic drugs, with a sample size of 120 for each, the mean values for LEDD, Levodopa, Pramipexole, Ropinirole, Rasagiline, Trihexyphenidyl, and Amantadine are 731.3, 458.6, 80.25, 15.33, 15.42, 132.5, and 29.17, respectively. The standard deviations range from 37.12 to 316.7, and the standard errors range from 3.389 to 28.91. In our study, we examined the effects of different dopaminergic drugs on cognitive impairment using the Stroop Reaction Test (SRT) and the Trail Making Test, which assess cognitive flexibility. In the Stroop test, we evaluated study subjects in two conditions: A-Congruent and B-Incongruent. In the A-Congruent condition, 68% of the subjects completed the test within 61 to 120 seconds, followed by 23% who finished in 0 to 60 seconds, 6% in 121 to 180 seconds,

2% in 241 to 300 seconds, and 1% in 181 to 240 seconds. In the B-Incongruent condition, most subjects (62%) completed the test within 60 to 180 seconds, followed by 21% who finished in 181 to 300 seconds, 6% in 301 to 420 seconds, 5% in 421 to 520 seconds, 4% in 541 to 660 seconds, 0.8% in 661 to 780 seconds, and 0.8% in 1141 to 1260 seconds. As per **Table 2** there is a significant negative correlation between SRT and **Levodopa** (p = 0.0363), with a 95% confidence interval ranging from -0.3583 to -0.0125.

Table 2: Pearson's correlation between SRT and Anti-parkinson's medication

TMT-A	Pearson's Correlation	Significance 2-tailed)	95% Confidence Interval	
			Lower	Lower
LEDD	0.09657	0.2941	-0.0841	-0.0841
LEVODOPA	-0.0181	0.8437	-0.1968	-0.1968
PRAMIPEXOLE	0.0511	0.5791	-0.1293	-0.1293
ROPINIROLE	-0.077	0.4024	-0.2529	-0.2529
RASAGILINE	0.0302	0.7430	-0.1498	-0.1498
TRIHEXYPHENIDYL	0.1720	0.0602	-0.007426	-0.007426
AMANTADINE	-0.09243	0.3153	-0.2672	-0.2672

In contrast, there is a significant positive correlation between SRT and Trihexyphenidyl (p = 0.0048), with a 95% confidence interval from -0.1832 to 0.1753. However, LEDD, Pramipexole, Ropinirole, Rasagiline, and Amantadine do not show a significant correlation with SRT, as indicated by their higher significance values. The Trail Making Test (TMT) consists of two parts: Trail A and Trail B. The mean scores for TMT-A and TMT-B in our study were 98.89 and 218.42, respectively. For TMT-A, the results revealed that 44% of the subjects completed the task within 60 to 120 seconds, followed by 32% who finished in 0 to 60 seconds, 15% in 121 to 180 seconds, 5% in 181 to 240 seconds, 1.6% in 240 to 360 seconds, and 0.8% in 361 to 420 seconds. Table 3 depicts that there was no significant correlation between **TMT-A** and any of the Anti-Parkinson's medications, as all significance values (p-values) are greater than the threshold of 0.05.

Table 3: Pearson's correlation between TMT-A and Anti-Parkinson's medications

SRT	Pearson's Correlation	Significance 2-tailed)	95% Confidence Interval	
			Lower	Lower
LEDD	-0.019	0.8326	-0.1980	-0.1980
LEVODOPA	-0.1913	0.0363	-0.3583	-0.3583
PRAMIPEXOLE	-0.1354	0.1404	-0.3072	-0.3072
ROPINIROLE	0.0143	0.8764	-0.1653	-0.1653
RASAGILINE	0.1229	0.1811	-0.0256	-0.0256
TRIHEXYPHENIDYL	0.2557	0.0048	-0.1832	-0.1832
AMANTADINE	-0.023	0.7968	-0.2452	-0.2452

Specifically, the correlation coefficients are close to zero, and the confidence intervals include zero, indicating no meaningful relationship between TMT-A and these medications. The data for TMT-B indicates a sample size of 120, with a mean score of 218.42, a standard deviation of 162.2, and a standard error of 14.8. There is no significant correlation between **TMT-B** and any of the Anti-Parkinson's medications, as all significance values (p-values) are greater than the threshold of 0.05. The correlation coefficients are close to zero, and the confidence intervals include zero, indicating no meaningful relationship between TMT-B and these medications as from **Table 4.**

Table 4: Pearson's correlation between TMT-B and Anti-Parkinson's medication

SRT	Pearson's Correlation	Significance 2-tailed)	95% Confidence Interval	
			Lower	Lower
LEDD	0.0330	0.7215	-0.1479	0.2118
LEVODOPA	0.0602	0.5153	-0.1211	0.2376
PRAMIPEXOLE	-0.0196	0.8319	-0.1990	0.1609
ROPINIROLE	0.0522	0.5722	-0.1289	0.2301
RASAGILINE	0.05189	0.5751	-0.1293	0.2297
TRIHEXYPHENIDYL	0.01152	0.9010	-0.1688	0.1911
AMANTADINE	-0.09237	0.3177	-0.2679	0.0891

Figure 4 represents different Impulse Control Diorders and Related Behaviours in the study population. It was found that highest percentage of study subjects had an impulsive behaviour associated with PD medication use.

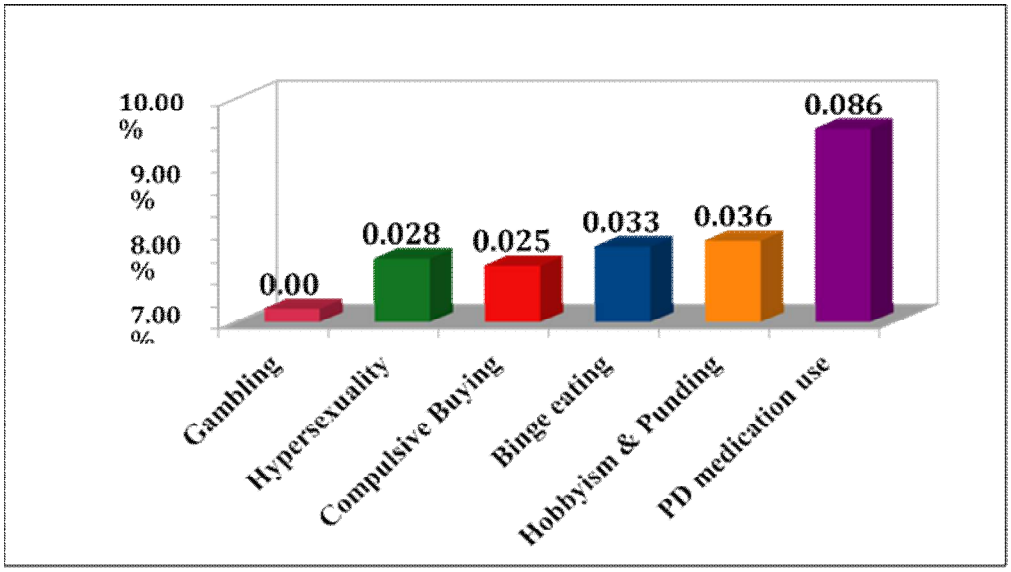

Figure 4: Impulse control disorders and related behaviours

Figure 5 represents the percentage of population with Total ICD, ICRB and QUIP-RS scores. ICRB's were found to be the highest among the study population. There was a significant correlation between **total ICD score** and **Pramipexole** (p = 0.0350), with a 95% confidence interval from -0.0138 to 0.3595. This suggested a weak, but significant, positive relationship between Pramipexole and the total ICD score. Other medications (LEDD, Levodopa, Ropinirole, Rasagiline, Trihexyphenidyl, and Amantadine) did not show significant correlations with the total ICD score as from **Table 5.**

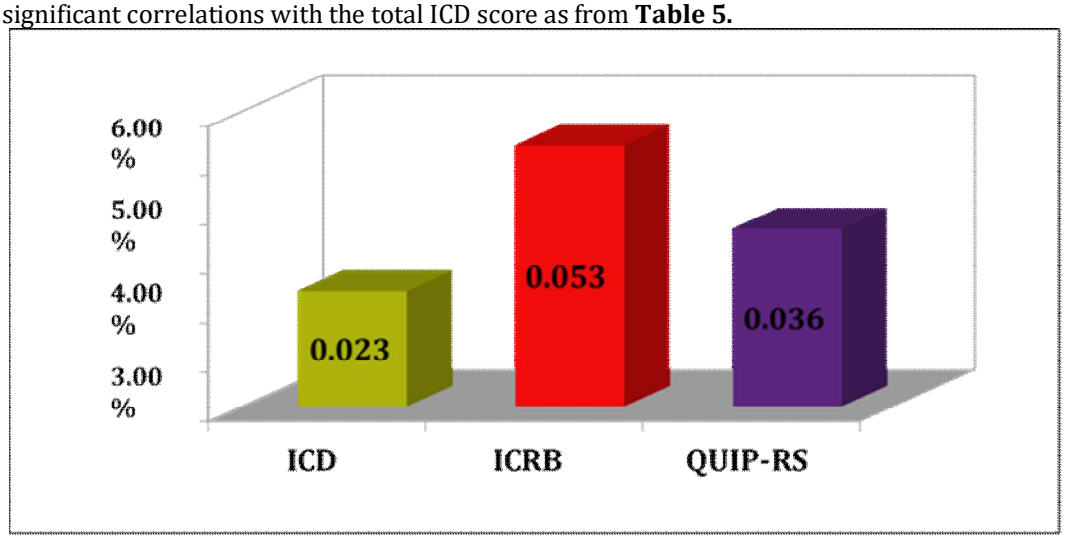

Figure 5: Percentage of population with Total ICD, ICRB and QUIP-RS scores

Table 5: Pearson's correlation between total ICD score and different dopaminergic drugs

SRT	Pearson's Correlation	Significance 2- tailed)	95% Confidence Interval	
			Lower	Lower
LEDD	0.0963	0.2953	-0.0843	0.2709
LEVODOPA	0.0047	0.9594	-0.1747	0.1838
PRAMIPEXOLE	0.1926	0.0350	-0.0138	0.3595
ROPINIROLE	0.0601	0.5142	-0.1204	0.2368
RASAGILINE	-0.1314	0.1526	-0.3035	0.04900
TRIHEXYPHENIDYL	-0.0004362	0.9962	-0.1797	0.1788
AMANTADINE	0.03373	0.7146	-0.1464	0.2117

Similarly, There, was a significant correlation between **total QUIP-RS score** and **Rasagiline** (p = 0.0278), with a 95% confidence interval from -0.3670 to -0.02251. This indicated a weak, but significant, negative

relationship between Rasagiline and the total QUIP-RS score. Other medications (LEDD, Levodopa, Pramipexole, Ropinirole, Trihexyphenidyl, and Amantadine) did not show significant correlations with the total QUIP-RS score as from **Table 6.**

Table 6: Pearson's correlation between total QUIP-RS and different dopaminergic drugs

SRT	Pearson's Correlation	Significance 2-tailed)	95% Confidence Interval	
			Lower	Lower
LEDD	0.1756	0.0551	-0.0037	0.3440
LEVODOPA	0.1592	0.0825	-0.02606	0.3290
PRAMIPEXOLE	0.0773	0.4009	-0.1033	0.2531
ROPINIROLE	0.0129	0.8884	-0.1667	0.1917
RASAGILINE	-0.2009	0.0278	-0.3670	-0.02251
TRIHEXYPHENIDYL	0.05960	0.5178	-0.1209	0.2363
AMANTADINE	0.04028	0.6622	-0.1400	0.2180

DISCUSSION

Impairment of cognition in PD typically emerges in more advanced stages, as neurodegeneration and the spread of Lewy bodies affect additional frontal-subcortical circuits, consisting of the dorsolateral prefrontal cortex, orbitofrontal cortex, and cingulate cortex [20-22]. The main area involved is cholinergic pathways and hence trihexiphendyl by blocking acetylcholine receptors may worsen this condition [23]. Reports have indicated that levodopa, along with other dopaminergic agonists like pramipexole and ropinirole, can improve attention span and cognition [24,25]. In our study, however, we found a statistically significant association with levodopa, but not with dopamine agonists. This may be due to the smaller number of patients using dopamine agonists in our study sample. The comparison of the prevalence of ICD and ICRB between the current study and other studies unveiled major differences. In the current study (N=120), 45% of participants had any ICD, which is higher than the prevalence reported in Sharma et al. [6] at 24.75%, Sharathchandra et al., [26] at 31.6%, and Auyeung et al., [27] at 7%. Regarding specific ICDs, hypersexuality was observed in 2.86% of participants in the current study, compared to 11.4% in Sharma et al., [8] 7.5% in Sharath chandra et al., [26] and 3.8% in Auyeung et al. [27]. Pathological gambling was found in 0.62% of subjects in the current study, lower than Sharma et al. (3.3%), Sharathchandra et al. (1.45%), and Auyeung et al. (6.1%). Compulsive eating was observed in 3.38% of participants in the current study, compared to 5.35% in Sharma et al., 7.8% in Sharathchandra et al., and 0.4% in Auyeung et al. Compulsive buying was found in 2.55% of the current study population, while it was higher in Sharma et al. (8.4%) and Sharathchandra et al. (8.2%), and 0.4% in Auyeung et al. Punding was reported in 3.64% of participants in the current study, higher than 12.4% in Sharma et al. and 15.4% in Sharathchandra et al. Compulsive medication use was observed in 8.64% of the current study, while it was 5.35% in Sharma et al. and 3.27% in Sharathchandra et al. Finally, 25% of subjects in the current study had two or more ICDs, compared to 15.7% in Sharma et al., 7.5% in Sharathchandra et al., and 3.7% in Auyeung et al. Previous studies have indicated a link between dopaminergic drugs and the development of ICD. Thr current study evaluated the impact of dopaminergic medications on the prevalence of ICDs. The findings revealed that the highest percentage of study subjects exhibited impulse behavior related to Parkinson's disease (PD) medication use (8.64%), followed by hobbyism and punding (3.64%), binge eating (3.38%), hypersexuality (2.8%), compulsive buying (2.55%), and gambling (0.6%). Additionally, the percentage of the study population with total ICDs, impulse control-related behaviors (ICRBs), and Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease–Rating Scale (QUIP-RS) scores were 2.35%, 5.31%, and 3.62%, respectively. The total mean score for ICDs was 1.5, while the mean QUIP-RS score was 4. Our study found that 45% of the participants exhibited at least one impulse control disorder (ICD). However, no significant correlation was observed between specific ICDs (gambling, hypersexuality, compulsive buying, or binge eating) and different dopaminergic drugs. A significant positive correlation was identified between hobbyism/punding and both LEDD and levodopa, indicating that higher doses of dopaminergic drugs and levodopa were associated with an increase in these behaviors. However, no significant correlation was found between overall Parkinson's disease (PD) medication use and dopaminergic drugs [28, 29]. Additionally, the study results showed a significant positive correlation between the total ICD score and the dopamine agonist pramipexole, suggesting its potential role in the development of ICDs. In contrast, a significant negative correlation was observed between the total QUIP-RS score and rasagiline, indicating a possible protective effect of rasagiline in reducing ICDs. This study provides a comprehensive analysis of cognitive impairment and impulse control disorders (ICDs) in Parkinson's disease (PD), contributing valuable insights into the effects of

dopaminergic medications [30]. The comparison with previous studies helps contextualize prevalence rates, while the use of validated assessment tools, such as the Stroop reaction test, Trail Making Test (TMT), and QUIP-RS, enhances the reliability of the findings. Significant associations between levodopa and cognitive function, as well as between pramipexole and ICDs, offer clinically relevant insights into medication effects. Additionally, the study identifies a potential protective role of rasagiline against ICDs, adding a novel perspective to existing research. However, certain limitations must be considered. The relatively small sample size (N=120) and unequal distribution of medication use may have limited the ability to detect significant associations, particularly for dopamine agonists. The cross-sectional design prevents causal inferences, and the lack of longitudinal data makes it difficult to assess the progression of cognitive impairment and ICDs over time. Self-reported behavioral assessments may introduce recall bias, and potential confounding factors, such as disease duration, psychiatric comorbidities, and concurrent medications, may not have been fully accounted for. Despite these limitations, the study provides valuable insights that can guide future research and clinical decision-making in PD management.

CONCLUSION

This study found PD to be more common in individuals aged 56 to 65 years, with a higher prevalence in males (67%) than females (33%). Only 16% of participants reported consanguineous parentage. Most subjects had an onset period of 1 to 5 years, and a significant correlation between disease onset and LEDD indicated that dopaminergic medication doses increased with progression of disease. The Unified Parkinson's Disease Rating Scale (UPDRS) revealed key findings: depression was the most prevalent symptom in UPDRS-I (mentation, behavior, and mood), handwriting was most affected in UPDRS-II (non-motor symptoms), and rigidity was highest in UPDRS-III (motor symptoms). Additionally, UPDRS-IV (complications of therapy) showed insomnia/hypersomnolence (38.3%) and dyskinesias (35.8%) as the most commonly reported issues. The Modified Hoehn and Yahr Staging scale indicated that the highest percentage (34%) of subjects were in stage 1.5, while the Schwab and England Activities of Daily Living Scale found that 25% of participants had a disability index of 70%. The PDQ-39 scale identified activities of daily living and mobility as the most affected quality of life domains. Levodopa was the mostly prescribed anti-Parkinsonism medication (97%). Cognitive assessments using the Stroop Reaction Test revealed a significant negative correlation between Stroop Reaction Time (SRT) and Levodopa, suggesting that Levodopa improves cognitive function, whereas a significant positive correlation between SRT and Trihexyphenidyl indicated that Trihexyphenidyl may contribute to cognitive decline. The study also evaluated the prevalence of ICD and impulse control-related behaviors (ICRBs), reporting rates of 0.6% for gambling, 2.86% for hypersexuality, 2.55% for compulsive buying, 3.38% for binge eating, 3.64% for hobbyism and punding, and 8.64% for PD medication.

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Competing Interest

None

Ethical Approval

The study was approved by the Institutional Review Board of Anurag university.

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