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IMPACT OF CNS DEPRESSANTS ON COGNITIVE FUNCTION IN PATIENTS WITH NEUROLOGICAL DISORDER AND COMORBIDITIES: A PROSPECTIVE CROSS-SECTIONAL STUDY

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Keywords:

Cognitive function, CNS Depressants, Neurological disorder, Comorbidities

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ABSTRACT: Background: Cognitive impairment is a serious problem, especially for the elderly. Cognitive impairment is often associated with neurological disorders and congenital diseases. The impact of central nervous system depressants (CNSDs) on cognition needs to be further investigated. **Objective:** This study aims to evaluate the relationship between CNSD use and cognitive impairment with neurological disorders and comorbidities, along with the severity of cognitive dysfunction. **Materials and Methods:** A prospective cross-sectional study was conducted over a 6-month period in a tertiary care hospital, including 129 patients aged 18 years and older. Cognitive function was assessed using a structured questionnaire and severity scales. Data on demographics, neurological disorders, medications, and comorbidities were collected from patient records and statistically analyzed. **Results:** Cognitive decline increased with age, particularly in patients aged 61+ years. Benzodiazepines were significantly associated with mild cognitive impairment. (22%, p = 0.02), while anti-convulsant and anti-Parkinsonian drugs had minimal impact. Stroke patients with comorbidities showed the highest rates of cognitive decline (25.3%, p = 0.01). **Conclusion:** The Results indicate that while CNS depressants may provide symptomatic relief, they also carry risks of further cognitive deterioration, particularly in vulnerable populations CNSDs, age, and comorbidities are key contributors to cognitive impairment. Early cognitive assessments and targeted management Strategies are crucial for improving outcomes. Further research is recommended. To establish causal links and explore long-term effects.

INTRODUCTION: Cognitive function is the mental process of acquiring knowledge and understanding through cognition, experience, and the senses. It includes processes such as knowledge, attention, memory, judgment and evaluation, problem solving and decision making, comprehension and production of language, etc. [1]. Increased age is linked to cognitive deterioration [2].

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Older patients have high levels of comorbidity, a higher risk of fall, disability, hospitalization, and early death due to genetic and environmental factors, and are consequently among the most frequent users of pharmacological treatment and may also lead to polypharmacy [3].

Age-related changes in physiology might impact the brain's homeostasis, blood-brain barrier permeability, neurochemistry, pharmacokinetics, and pharmacodynamics of drugs and increase the potential for adverse events in older adults [4, 5]. Many medications can have deleterious effects on cholinergic and dopaminergic pathways [6]. Cognitive deficiencies can be inherited or later brought on by external factors such as neurological

illnesses, mental illness, or brain injuries. Cognitive impairments can occur at any age due to head injuries, brain infections, or meningitis. Cognitive impairment can be brought on by a number of disorders as people age, including stroke, delirium, dementia, depression, schizophrenia, persistent alcohol use, substance addiction, brain tumors, vitamin deficiencies, hormonal imbalances, and some chronic diseases. Cognitive deficiencies can be a symptom of brain diseases such as Alzheimer's, Parkinson's, Lewy body, Huntington's, and HIV dementia [7]. Other examples include immunological disorders like systemic lupus erythematosus, metabolic disorders, autism, heavy metal toxicity, malnourishment, and side effects of cancer treatment. Cognitive impairments are also linked to medications such as sedatives, tranquilizers, anticholinergics, and glucocorticoids. They are benzodiazepines, barbiturates, opioids, antiepileptic drugs, anticholinergics, antipsychotics, antidepressants, muscle relaxants, stimulant drugs, antihistamines, and tricyclic antidepressants.

Benzodiazepines, barbiturates, Z-hypnotics, opioids These are drugs taken long-term; usage can result in issues with withdrawal symptoms, abuse, cognitive impairment, and associated dementia risks, depressive symptoms, and paradoxical effects such as disinhibition, anxiety, impulsivity, and troubles stopping the medication [8, 9, 10].

Antiepileptic drugs like phenytoin (PHT), carbamazepine (CBZ), valproate (VPA), phenobarbital (PB), and benzodiazepines have been used in epilepsy treatment for many years and are categorized as older AED treatments. Taking long-term to produce little change in cognition after AEDs and with PB producing greater cognitive impairment. Many newer AEDs have been introduced since the early 1990s, including gabapentin (GBP), lamotrigine (LTG), topiramate (TPM), vigabatrin (VGB), pregabalin (PGB), and levetiracetam. To compare the older to produce the minimum side effects [11]. Medications with anticholinergic properties, such as some antihistamines (e.g., diphenhydramine), tricyclic antidepressants (e.g., amitriptyline), and some bladder medications, can negatively impact cognitive function, particularly in older adults [12-14]. As more medications are prescribed, the likelihood of drug-induced disorientation rises. Additionally, polypharmacy increases the risk of medication errors and interactions. Consequently, aged Individuals should take fewer nonessential medications. Special care is needed for people with pre-existing cognitive impairment. Especially psychoactive drugs and anticholinergic drugs should be avoided. It is easy to overlook mild cognitive impairment in a crowded ward or clinic. Routine use of brief mental test scores not only improves detection of cognitive deficits but provides a baseline against which possible changes can be measured [15].

The primary aim of a prospective cross-sectional study was to examine the effect of cognitive function-associated neurological disorder with its comorbidity patients by using CNS depressant medication. Given the increasing population of cognitive impairment in aging populations and the widespread use of CNS depressants, understanding their impact on cognitive health is critical. A secondary objective was to assess the severity of cognitive dysfunction associated with CNS depressants using patients. Therefore, Routine clinical cognitive tests are used in our hospital wards.

MATERIALS AND METHODS:

Study Design and Settings: We performed a prospective cross-sectional study of 129 patients in somatic wards of a tertiary care hospital in Erode district, Tamil Nadu. The hospital has a vast inclusion area for both rural and urban areas. The entire study was conducted over 6 months (March 2024 - August 2024: duration of follow-ups to assess the severity. The patients were included consecutively, at one or two days of their stay at Maruthi medical center hospital (Erode), from the Neurology, General Internal Medicine, departments. Data were gathered using interviews, tests, questionnaires, and an electronic patient record (EPR).

Participants: All 129 patients from the original perspective cross-sectional study were included. Inclusion Criteria were we included the patients. Over the age of 18 years and all genders. Inpatients under CNS depressants medications along with the underlying diseases, such categories with extra CNS associated medical conditions in admitted on neurological department in tertiary care hospital.

Exclusion Criteria were pregnant and lactating women, psychosis, patients/bystanders who were not interested in taking part in our research. We excluded patients with a GCS (Glasgow coma scale) less than 7 to avoid the inclusion of patients with reduced consent ability.

Study Procedure: At the initial stage of the study, a self-structured questionnaire has been designed and prepared. And all the patients were requested to fill out the validated data collection form. Data follow-up will be collected from the medical record department. Firstly, after the collection of the patient's data, we evaluate the differences between the cognitive function and the associated neurological disorder with its comorbidities. Secondly, submitting the severity assessed using the severity assessment scale.

Data Collection: History of neurological disorder, comorbidities, and CNSD use was collected from participants, the general practitioners (GPs) medication lists, and the EPR. We collect the information on medication type/name that was provided by the caretaker, CNSD. Medication use was defined as using opioids, BZDs, Z-hypnotics, and anticholinergics. Barbiturates, anti-epileptics, anti-psychotics, anti-Parkinson's, or a combination of them and how many days of taking in before hospital admission in patient. We are used the date collection form and collected the sociodemographic data as well as reasons for admission, clinical diagnoses, and comorbidities. Firstly, collect the clinical data, including patient general behaviour, perception, Feelings, thought processes, and memory are required information to collect. using the Glasgow Coma Scale (GCS). Secondly, to assess the severity by using the cognitive severity assessment scale. Occasionally, the author should follow up. The participants and collect the data. Who taught the collecting writers how to Use the standard cognitive tests as well.

Cognitive outcome Measures: A self-assessment questionnaire is a screening instrument for cognitive impairment. This tool is made based on positive psychology. The standardized guide that provided guidance on administering and interpreting the test was utilized. This questionnaire takes approximately between 15 and 20 minutes to perform and addresses general domains (eye contact, posture, motor activity, facial expression, speech volume, state of consciousness) and major domains (perception, feeling, thought processes, memory, misplace things). This tool can be used to examine cognitive profiles in different populations of patients, including dementia, mild cognitive impairment, psychiatric illness, and substance abuse. On the other hand, severity assessment tool is used to assess the cognitive severity. This tool is made based on the GCS scale. Overall, the GCS score is 15. These scales (No, very mild, mild, moderate, moderately severe, severe, and very severe cognitive decline used to determine the cognitive score. The primary outcome was severity of cognitive dysfunction associated with CNS depressants using patients.

Ethics: This the study involved participants who signed informed consent at baseline. The Data was stored on a secure server by the author. The data collection and storage were approved by the ethical committee.

Statistical Analysis: The statistical analysis was conducted. Using IBM SPSS Statistics software (IBM Corp, released 2015, IBM SPSS Statistics for Windows, V.23.0. Armonk, NY, USA). The distribution of continuous data was evaluated. graphically by analyzing the histograms (age, gender). Age vs. severity, drug vs. severity and comorbidity vs. severity). Descriptive statistics were employed to Summarize the data. Continuous variables (e.g., age) were presented as means and standard deviations (SD), while categorical variables (e.g., gender, age) were summarized as frequencies and percentages. The main outcome was the effect of cognitive function associated neurological disorder with its comorbidity patients by Using CNS depressants, medication is defined as the mean score of multidimensional Cognistat test. The secondary outcome was assessing the severity of cognitive function were mean scores of the routine tests (severity assessment scale). Comparative analyses were performed using chi-square (χ^2) tests to assess the associations between cognitive impairment and the independent variables. Statistical significance was determined by a p-value < 0.05. To account for potential Confounding factors, such as age, gender, drugs, and comorbidities, are these: Covariates were included in the analysis.

Adjusted chi-square tests were used to determine the relationship between cognitive impairment and the independent variables. All analyses adhered to standard statistical procedures to ensure reliability and validity. The results demonstrated statistically significant relationships, highlighting the impact of the variables on cognitive impairment.

RESULTS:

TABLE 1: PATIENT DEMOGRAPHICS AND CHARACTERISTICS

Parameter	Value
Total patients	129 P
Age distribution	
31-40	7 patients (5.4%)
41-50	16 patients (12.6%)
51-60	40 patients (30.7%)
61-70	45 patients (34.7%)
Above 71	21 patients (16.7%)
Gender distribution	
Male	72 patients
Female	57 patients
Neurological disorder	
Stroke	31 patients (24%)
Parkinson's	15 patients (12%)
Seizures	20 patients (15.5%)
Comorbid	63 patients (48.5%)

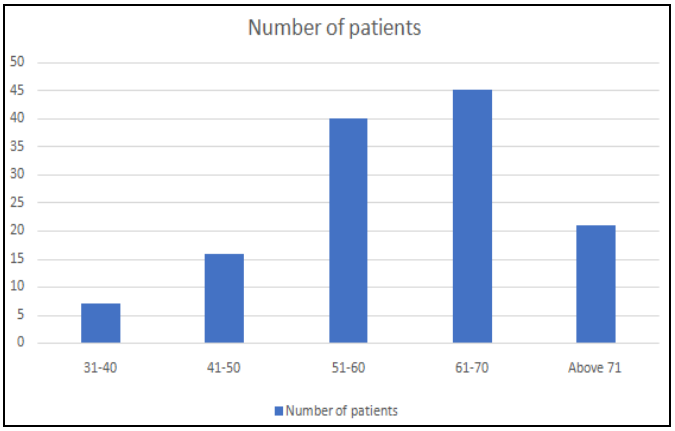

FIG. 1: AGE DISTRIBUTION PATTERNS (N=129)

The study included 129 patients, predominantly aged 61-70 years (34.7%), with 30.7% aged 51-60 years and 16.7% above 71 years. Male patients comprised 55.8% of the sample, while females accounted for 44.2%.

Neurological disorders such as stroke (24%), Parkinson's disease (12%), and seizures (15.5%) were common. Comorbidities were prevalent, affecting 48.5% of the participants, with stroke patients experiencing the highest burden.

TABLE 2: AGE VS COGNITIVE IMPAIRMENT SEVERITY (1ST AND 2ND REVIEW)

Age	NCI	VMCI	MCI	MOCI
Severity		**1st Review**		
31-40 Years	4 (3.1%)	1 (0.8%)	2(10.6%)	0(0%)
41-50 Years	7 (5.4%)	4 (3.1%)	3(2.3%)	0(0%)
51-60 Years	10 (7.7%)	7 (6.2%)	11(8.5%)	1(0.8)
61-70 Years	5 (3.9%)	10 (7.7%)	9(7%)	3(2.3%)
71+ Years	1 (0.7%)	5 (3.9%)	4 (3.1%)	2(1.6%)
		2nd Review		
31-40 Years	0 (0%)	3(2.3%)	0(0%)	0(0%)
41-50 Years	4 (3.1%)	8(6.2%)	6(4.7%)	0(0%)
51-60 Years	6 (4.7%)	8(6.2%)	9(7%)	2(1.6%)
61-70 Years	2 (1.5%)	14 (10.8%)	8(6.2%)	5(3.9%)
71+ Years	0 (0%)	5 (3.9%)	3(2.3%)	2(1.6%)
P-Value	0.01	0.03	0.05	0.08

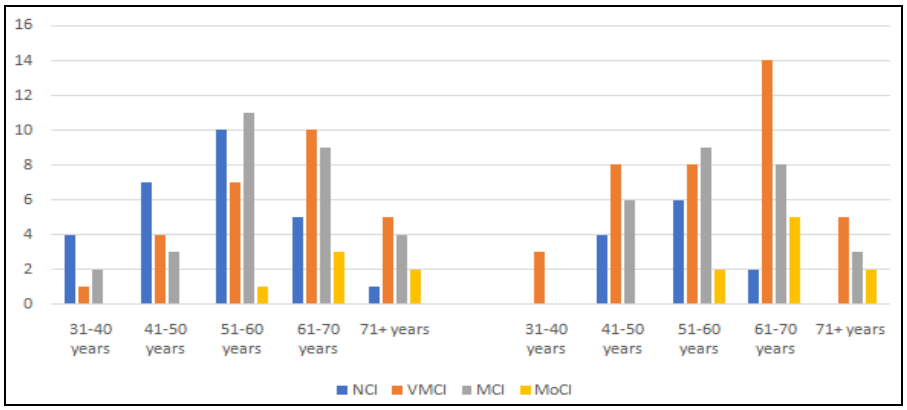

FIG. 2: AGE VS SEVERITY (1ST REVIEW VS 2ND REVIEW)

Our investigation revealed that patients aged 61 or older had significantly higher levels of cognitive impairment. Mild cognitive impairment (MCI) was more common in patients aged 71 and up in the second evaluation (p = 0.05), while moderate cognitive impairment (MoCI) was more common in older age groups, with statistical significance (p = 0.08). These findings underscore the role of aging in cognitive deterioration.

TABLE 3: COGNITIVE EFFECTS OF MEDICATIONS (1ST AND 2ND REVIEW)

Medication Severity	BZD	Anti-Convulsants	Anti-Convulsants +Zolpidem	Zolpidem	Anti-Parkinsonian Drugs
			1st Review		
NCI	5(4%)	22(17%)	0(0%)	1(0.8%)	2 (1.6%)
VMCI	15(11.6%)	1(0.8%)	11(8.5%)	3(2.3%)	9 (7%)
MCI	27 (20%)	0 (0%)	14 (10.9%)	7 (5.4)	12 (9.3%)
MOCI	4 (3.1)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
			2nd Review		
NCI	5 (3.9%)	22 (17%)	0 (0%)	2 (1.6%)	2 (1.6%)
VMCI	15 (11.6%)	1 (0.8%)	11(8.5%)	6 (4.7%)	9 (7%)
MCI	28 (21.7%)	0 (0%)	14 (10.9%)	7 (5.4%)	12 (9.3%)
MOCI	3 (2.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
P-Value	0.02	0.04	0.03	0.05	0.02

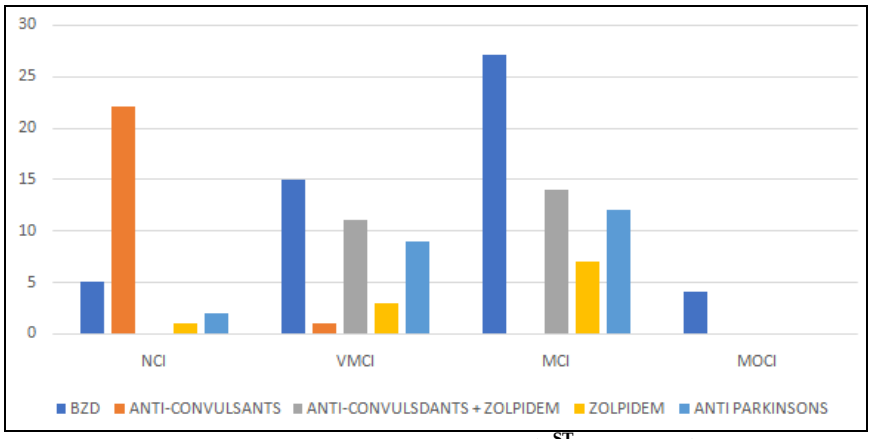

FIG. 3: DRUG VS SEVERITY (1ST REVIEW)

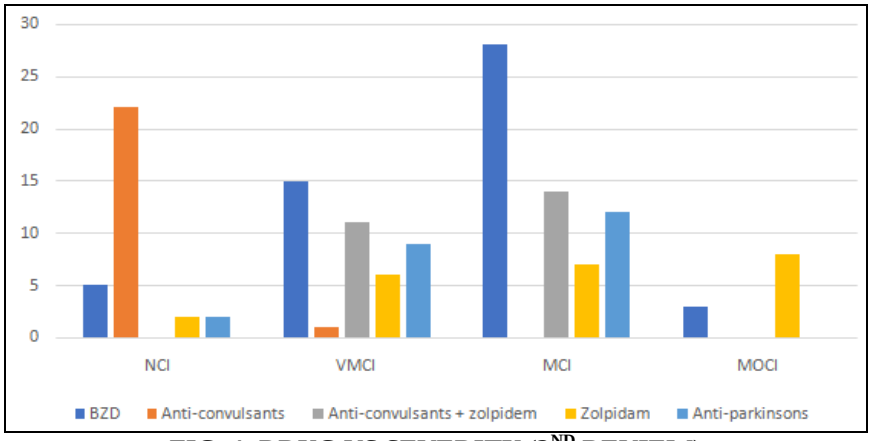

FIG. 4: DRUG VS SEVERITY (2ND REVIEW)

The medication analysis for our study found that benzodiazepines (BZDs) were more substantially related to cognitive decline than other drugs, contributing to mild cognitive impairment in 22% of patients (p = 0.02). The Zolpidem medication used in patients also had a modest effect on cognitive decline (p=0.05), whereas anti-convulsants had a negligible influence on cognition when compared to BZDs (p-value = 0.04). Anti-Parkinsonian medicines had modest cognitive effects (p = 0.02), indicating a safer profile for cognitive outcomes.

TABLE 4: COMORBID VS SEVERITY (1ST VS 2ND REVIEW)

Condition	NCI	VMCI	MCI	MOCI	NCI	VMCI	MCI	MOCI	P= value
	(1st Review)				(2nd Review)				
Parkinson's+ comorbidity	0 (0%)	2(1.6%)	5(3.8%)	0(0%)	0(0%)	1(0.8%)	6(4.7%)	0(0%)	0.04
Seizure + comorbidity	0 (0%)	13(10%)	0(0%)	0(0%)	0(0%)	6(4.7%)	7(5.4%)	0(0%)	0.05
Stroke + comorbidity	1(0.7%)	28(22%)	14(11%)	0(0%)	0(0%)	5(3.9%)	33(25.3%)	7(4.7%)	0.01

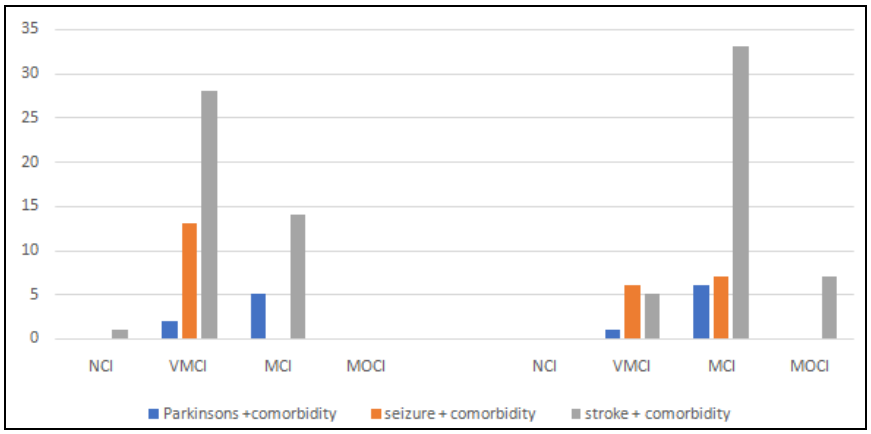

FIG. 5: COMORBIDITY VS SEVERITY

Patients with comorbidities had more severe cognitive deterioration. Stroke patients with coexisting illnesses such as diabetes and hypertension saw the highest rate of cognitive deterioration. In the second review, 25.3% of stroke patients with comorbidities developed mild cognitive impairment ($p = 0.01$). Parkinson's disease patients with comorbidities also experienced considerable cognitive decline, with mild cognitive impairment rising from 3.8% to 4.7% during the second evaluation ($p = 0.04$). Similarly, patients with seizures and Comorbidities had lower cognitive outcomes ($p = 0.05$). While substantially better in other neurological health conditions.

DISCUSSION: This study investigated the relationship between the use of CNS depressants medication (such as opioids, BZDs, Z-hypnotics, anticonvulsants, and anti-Parkinson's) drug) and cognitive impairment in patients with neurological disorder and associated comorbidities. The first finding was the effect of cognitive function. measured by using the questionnaire form. A secondary objective was to assess severity of cognitive dysfunction associated with CNS depressants using patients. We also investigated the connection among cognitive function, CNSDs, and comorbidities. CNSD use was associated with worse cognitive outcomes in the group with high comorbidity and age-related increase in cognitive impairment, with older patients (61+ years) showing the most severe cognitive decline. This finding reinforces the need for early cognitive assessments and interventions for aging populations, particularly those with neurological conditions. This observation is consistent with previous literature, which associates aging with physiological changes such as decreased brain homeostasis, altered pharmacokinetics and neurochemical imbalances that exacerbate cognitive deficits [1].

Our study found that the majority of benzodiazepine users had moderate cognitive impairment, particularly in the second review, which indicated a significant decline in cognitive function ($p = 0.02$). This highlights the potential risks. of memory loss and reliance linked to long-term benzodiazepine use in people with neurological disorders, according to Olfson *et al.* (2015). Even at lower dosages, BZD-induced cognitive decline has a substantial influence on memory and executive function, especially in the older population, according to Marketa Marvanova *et al.* (2016) [5]. Siddiqui *et al.* (2020) [3], among older

hospitalized patients, global cognition, and specific cognitive functions were associated with long-term use of CNSD medication as well as with somatic comorbidity.

On the other hand, the neuroprotective potential of anticonvulsants and anti-Parkinsonian medications were suggested by their comparatively low cognitive impact [12]. Highlighted the tailored use of anti-parkinsonian drug in minimizing cognitive risk, particularly in managing neurodegenerative conditions. These results are consistent with those of Perk *et al.* (2008) [11], who observed that when compared to older medications like phenobarbital, newer anticonvulsants like gabapentin, and Lamotrigine has fewer cognitive side effects.

According to our findings, stroke patients with concomitant conditions such as diabetes and hypertension saw the greatest rate of cognitive decline. In the second review, 25.3% of stroke patients with comorbidities progressed to mild cognitive impairment ($p = 0.01$). Marvanova (2016) discusses that vascular Comorbidities such as diabetes and hypertension exacerbate cognitive impairment. By lowering cerebral blood flow and increasing oxidative stress.

According to our findings, the second review of Parkinson's disease with comorbid condition also found a significant increase in mild cognitive impairment (from 3.8% to 4.7%) ($p = 0.04$), showing that cognitive impairment is more likely to occur in Parkinson's disease patients who also have other illnesses. This is in line with findings from Alkattan *et al.* (2021) [8], which linked inflammatory and metabolic factors to worsened cognitive outcomes in Parkinson's disease.

While this study is retrospective; longitudinal studies with higher sample sizes are required to demonstrate stronger causal relationships between comorbid illnesses, drugs, and cognitive impairment. Further research should also explore the long-term effects of anti-Parkinsonian drugs and anticonvulsants on cognitive health.

CONCLUSION: The study contributes valuable insights into the nuanced relationship between the neurological disorder, comorbidities and CNSD use may affect cognitive function. Our study highlights the need for early intervention strategies to manage the comorbidity and monitor the medication effects, ensuring a better cognitive outcome for patients with neurological disorder. It is crucial for prescribing physicians and other healthcare professionals to be aware of the potential cognitive side effects of CNSD drugs in older patients with comorbidity. This is done to inform patients and their next of kin. Comprehensive Neuropsychological testing could be helpful in describing cognitive impairment. Associated with drug and illness burden.

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