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EVALUATION OF BENZODIAZEPINE DEPENDANCE AND ITS ASSOCIATION WITH COAGNITIVE FUNCTIONING IN LONG TERM USERS AT RAMA MEDICAL COLLEGE AND RESEARCH CENTRE, KANPUR

Dr. Puneeta Sharma[1], Dr. Debasish Padhi[2], Dr. Priyanka Shukla[3]

Affiliation

[1] Junior Resident, Department of Psychiatry, Rama Medical College Hospital and Research Centre, Kanpur

[2]Associate Professor, Department of Psychiatry, Rama Medical College Hospital and Research Centre, Kanpur

3 Associate Professor & HoD, Department of Clinical Psychology, CSJM University, Kanpur

Corresponding Author: Dr. Puneeta Sharma, puneeta16099sharma@gmail.com

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ABSTRACT

Background:

Long-term benzodiazepine (BZD) use has been associated with cognitive decline, but the relationship between dependence severity and specific cognitive domains remains underexplored. This study aimed to assess the extent of benzodiazepine dependence and its impact on cognitive functioning in chronic users.

Materials and Methods

A cross-sectional study was conducted on 120 long-term BZD users (≥6 months) at Rama Medical College Hospital and Research Centre, Kanpur. Participants were assessed using the Benzodiazepine Dependence Self-Report Questionnaire (BENDEP-SRQ), which covers four domains (problematic use, preoccupation, lack of compliance, and withdrawal symptoms), and the Montreal Cognitive Assessment (MoCA) for cognitive evaluation. Sociodemographic details were also collected. Data analysis was done using SPSS version 29.2, with Pearson correlation used to determine associations.

Results

A majority of participants were male (60%), aged 36–39 years (49.2%), from low socioeconomic backgrounds (61.7%), and had only primary education (50.8%). The severity of benzodiazepine dependence was significantly associated with cognitive impairment. A strong negative correlation was found between dependence severity and MoCA total score ($r = -0.887$, $p < 0.001$), with specific domains such as attention ($r = -0.885$) and delayed recall ($r = -0.833$) being most affected. The moderate dependence group showed the highest frequency of high scores in BENDEP domains, particularly in problematic use and preoccupation.

Conclusion

Benzodiazepine dependence is strongly associated with cognitive decline, especially in attention, memory, and overall cognitive functioning. Sociodemographic vulnerabilities—such as male gender, low education, and low income—further compound this risk. Routine cognitive screening and timely intervention in long-term BZD users are essential to mitigate the risk of irreversible cognitive impairment.

INTRODUCTION

Benzodiazepines have been a cornerstone in the treatment of anxiety disorders, insomnia, seizures, muscle spasms, and alcohol withdrawal since their introduction in the 1960s. Their popularity stems from their efficacy, rapid onset of action, and relatively favorable short-term safety profile [1]. Despite these advantages, concerns have increasingly arisen about their long-term use, which can lead to dependence, tolerance, and withdrawal symptoms [2].

Dependence on benzodiazepines can occur even when they are used within therapeutic limits, and this risk increases significantly with prolonged use [3]. Patients may develop both psychological dependence—characterized by preoccupation and craving—and physical dependence, which includes tolerance and withdrawal symptoms upon dose reduction or discontinuation [4]. These effects often go unrecognized in routine clinical settings, particularly when patients continue their medication for months or even years without reassessment [5].

Long-term use of benzodiazepines has also been linked to a range of cognitive deficits. These include impairments in memory, processing speed, attention, and executive functioning [6]. Several studies have demonstrated that chronic users perform worse than controls in tasks involving delayed recall, verbal learning, and psychomotor coordination [7]. These cognitive deficits can significantly impact daily functioning and may increase the risk of accidents, decreased work efficiency, and reduced quality of life [8].

Furthermore, benzodiazepine-related cognitive impairment may not always be reversible. While some users recover their cognitive abilities after discontinuation, others continue to show persistent deficits, particularly in memory and processing speed [9]. This has been attributed to the long-term suppression of central nervous system activity through enhanced GABAergic transmission, potentially leading to neuroplastic changes in regions such as the hippocampus and prefrontal cortex [10].

Emerging evidence also suggests that benzodiazepine use may be associated with an increased risk of developing dementia or mild cognitive impairment, especially among older adults [11]. While age is a significant risk factor in itself, prolonged use of sedatives may exacerbate cognitive decline or mask its early signs [12]. Therefore, evaluating the extent of cognitive impairment in long-term users is not only clinically relevant but may also have implications for early detection of neurodegenerative processes.

Although the association between long-term benzodiazepine use and cognitive decline is well documented, relatively few studies have examined whether the **severity of dependence** itself correlates with the degree of cognitive impairment. Some researchers have proposed that individuals with more severe dependence—characterized by higher doses, longer durations, and stronger psychological attachment—may exhibit more pronounced cognitive deficits [13]. However, this hypothesis has yet to be comprehensively validated through structured dependence assessment tools and objective cognitive testing.

One study by Boeuf-Cazou and colleagues assessed the cognitive functioning of young adults using benzodiazepines and found significant impairments in verbal memory, particularly among women [14]. Another study by Zetsen et al. evaluated long-term benzodiazepine users and reported that nearly 21% showed measurable cognitive impairment, with attention, executive function, and processing speed most affected [15]. These findings underline the importance of examining the relationship between **dependence severity** and specific cognitive domains.

In the clinical context, benzodiazepine use is often overlooked when patients present with subtle cognitive complaints. As a result, dependence may remain undiagnosed and its impact on cognition underestimated. This highlights the need for validated tools to assess dependence and structured cognitive evaluation in long-

term users. Identifying patterns of dependence that are linked to cognitive decline can help clinicians in making informed decisions regarding tapering, switching to alternatives, or introducing cognitive rehabilitation interventions [16].

This study aims to evaluate the level of benzodiazepine dependence and its association with cognitive performance in long-term users. By investigating this relationship, the study seeks to contribute to a more nuanced understanding of benzodiazepine-related cognitive risks and support safer prescribing practices, particularly in vulnerable populations.

MATERIAL AND METHOD

This was a cross-sectional observational study conducted at the Department of Psychiatry, Rama Medical College Hospital and Research Centre, Kanpur. The objective of the study was to evaluate benzodiazepine dependence and its association with cognitive functioning among long-term users. A total of 120 participants were recruited through purposive sampling. The sample size was determined based on feasibility and the goal of exceeding the typical sample sizes used in previous studies on long-term benzodiazepine use and cognitive functioning, which reported mean sample sizes ranging from 29 to 93 participants. Compared to prior studies, our sample size provides improved statistical power to detect meaningful associations between benzodiazepine dependence and cognitive performance. All participants were aged 18 years or above and had been consuming benzodiazepines continuously for at least six months prior to enrollment in the study.

Participants were included if they met the following criteria: age 18 years or older, continuous use of benzodiazepines for a minimum of six months, and willingness to provide written informed consent. Individuals were excluded if they had a diagnosis of major psychiatric illness such as schizophrenia, bipolar disorder, or other psychotic disorders, a history of neurological disorders such as stroke, epilepsy, or dementia, or if they were using other central nervous system (CNS) depressants, including opioids or alcohol.

After obtaining written informed consent, all participants underwent a structured clinical interview. Sociodemographic and clinical information was recorded using a semi-structured proforma. Participants were then assessed using two standardized tools: the Benzodiazepine Dependence Self-Report Questionnaire (Bendep-SRQ) and the Montreal Cognitive Assessment (MoCA).

The Bendep-SRQ is a validated self-report instrument used to assess the degree and characteristics of benzodiazepine dependence. It comprises 20 items distributed across four domains: problematic use (6 items), preoccupation (5 items), lack of compliance (4 items), and withdrawal symptoms (5 items). Each item is rated on a 5-point Likert scale ranging from "never" to "always," scored from 0 to 4. Domain scores range from 0 to 25, with higher scores indicating greater levels of dependence. This multidimensional tool enables a comprehensive evaluation of both behavioral and psychological aspects of benzodiazepine use.

The Montreal Cognitive Assessment (MoCA) is a widely used cognitive screening tool designed to detect mild cognitive impairment. It evaluates multiple cognitive domains, including attention and concentration, executive functions, memory, language, visuospatial skills, abstract thinking, calculations, and orientation. The tool consists of 30 items, with a maximum total score of 30 points. The scoring is distributed across domains as follows: visuospatial/executive function (5 points), naming (3 points), attention (6 points), language (3 points), abstraction (2 points), delayed recall (5 points), and orientation (6 points). A score below 26 is generally considered indicative of cognitive impairment. The MoCA is sensitive to subtle cognitive deficits and is especially useful in detecting early stages of cognitive decline.

The collected data were analyzed using IBM SPSS Statistics version 29.2 for Windows. Sociodemographic characteristics and clinical variables were summarized using descriptive statistics, presented as frequencies and percentages for categorical variables, and means with standard deviations for continuous variables. The association between benzodiazepine dependence severity and cognitive functioning was assessed using the Pearson correlation coefficient. This statistical test was also applied to explore relationships between sociodemographic factors, dependence severity, and MoCA scores. A p-value of less than 0.05 was considered

statistically significant.

The study received approval from the Institutional Ethics Committee of Rama Medical College, Kanpur. All participants were informed in detail about the study's aims, procedures, and confidentiality measures. Written informed consent was obtained from each participant before data collection. Confidentiality and anonymity were strictly maintained throughout the research process.

RESULTS

Table 1: Sociodemographic Profile of Participants (N = 120)

Variable	Category	Frequency (n)
Sex	Male	72
	Female	48
Socioeconomic Status	Low	74
	Middle	41
	High	5
Education Level	Primary	61
	Secondary	42
	Higher	17
Marital Status	Married	93
	Unmarried	27
Age Group	Late 30s (36–39)	59
	Early 40s (40–44)	36
	Late 20s (26–29)	25

Table 1 summarizes the sociodemographic characteristics of the study participants. Out of 120 participants, 60% were male (n = 72) and 40% were female (n = 48). The majority belonged to the low socioeconomic status group (61.7%), followed by middle (34.2%) and high (4.1%) income groups. Regarding education, most participants had completed only primary education (50.8%), while 35.0% had secondary education and only 14.2% attained higher education. A large proportion of participants were married (77.5%), with the remaining 22.5% unmarried. In terms of age distribution, the late 30s age group (36–39 years) constituted the largest segment (49.2%), followed by early 40s (30%) and late 20s (20.8%).

Table 2: Number of Patients with High BENDEP Domain Scores by Dependence Level

BENDEP Domain	Mild Dependence	Moderate Dependence	Severe Dependence
Problematic Use	12	34	11
Preoccupation	8	32	11
Lack of Compliance	14	28	10
Withdrawal Symptoms	13	30	11

Table 2 presents the number of patients exhibiting high domain scores on the BENDEP-SRQ across varying levels of benzodiazepine dependence (mild, moderate, and severe). The **moderate dependence group** showed the highest frequency of elevated scores across all four BENDEP domains: **problematic use (n = 34)**, **preoccupation (n = 32)**, **lack of compliance (n = 28)**, and **withdrawal symptoms (n = 30)**. In comparison, the **mild dependence group** demonstrated lower domain scores, with **problematic use (n = 12)**, **preoccupation (n = 8)**, **lack of compliance (n = 14)**, and **withdrawal symptoms (n = 13)**. Interestingly, the **severe dependence group** recorded a slight decrease in high domain scores relative to the moderate group, with all domains ranging between **n = 10 to 11**. This pattern indicates that **problematic and compulsive behaviors associated with benzodiazepine use are most prominent in the moderate dependence group**, potentially reflecting increased insight and reporting before the onset of greater cognitive impairment observed in severe cases.

Table-3 MoCA Domain Scores by Dependence Level

Domain	Mild	Moderate	Severe	p-value
Attention	5.34 ± 0.59	3.97 ± 0.71	1.76 ± 0.60	<0.001*
Visuospatial Executive	4.23 ± 0.70	3.10 ± 1.12	1.80 ± 1.08	<0.001*
Naming	2.79 ± 0.41	2.75 ± 0.53	2.48 ± 0.59	0.06
Delayed Recall	4.14 ± 0.47	2.72 ± 0.79	1.38 ± 0.63	<0.001*
Language	2.90 ± 0.31	2.84 ± 0.48	2.65 ± 0.49	0.124
Abstraction	1.76 ± 0.44	1.66 ± 0.51	1.61 ± 0.50	0.519
Orientation	5.38 ± 0.73	5.32 ± 0.70	5.04 ± 0.77	0.199
MoCA Total	27.14 ± 1.30	22.37 ± 2.04	16.13 ± 1.84	<0.001*

Table 3 presents the comparison of MoCA domain scores across levels of benzodiazepine dependence severity (mild, moderate, severe). A significant decline in cognitive performance was observed with increasing dependence severity. The most pronounced impairments were seen in attention, visuospatial/executive

functioning, delayed recall, and the MoCA total score, all showing statistically significant differences ($p < 0.001$). For instance, the mean attention score dropped from 5.34 ± 0.59 in the mild group to 1.76 ± 0.60 in the severe group. Other domains such as naming, language, abstraction, and orientation did not show statistically significant differences across dependence groups.

Table-4 Correlation Between Dependence Severity and MoCA Domains

MoCA Domain	Correlation (r)	p-value
Attention	-0.885	<0.001*
Visuospatial Executive	-0.671	<0.001*
Naming	-0.188	0.040 *
Delayed Recall	-0.833	<0.001*
Language	-0.173	0.058
Abstraction	-0.103	0.262
Orientation	-0.146	0.111
MoCA Total	-0.887	<0.001*

Correlation analysis between dependence severity and MoCA domains (Table-4) revealed a strong and statistically significant negative correlation with several cognitive domains. Attention showed the highest negative correlation ($r = -0.885$, $p < 0.001$), followed closely by MoCA total score ($r = -0.887$, $p < 0.001$) and delayed recall ($r = -0.833$, $p < 0.001$). A moderate negative correlation was also found in the visuospatial executive domain ($r = -0.671$, $p < 0.001$). A weaker, but statistically significant correlation was observed with naming ($r = -0.188$, $p = 0.040$). Other domains such as language, abstraction, and orientation did not show statistically

significant associations with dependence severity. These findings suggest that increasing benzodiazepine dependence severity is particularly associated with impairments in attention, memory, and executive functioning, as well as overall cognitive performance.

DISCUSSION

The study aimed to evaluate the association between benzodiazepine dependence and cognitive functioning using the BENDEP-SRQ and MoCA scales. A clear pattern emerged showing that as the severity of dependence increased, cognitive performance—especially in attention, executive function, and memory (delayed recall)—declined significantly. This finding aligns with existing literature indicating that long-term benzodiazepine use is associated with impairments in working memory, processing speed, and attention regulation [17,18].

A strong negative correlation was observed between dependence severity and MoCA total score ($r = -0.887$, $p < 0.001$), as well as between attention ($r = -0.885$) and delayed recall ($r = -0.833$). These results support the hypothesis that benzodiazepine dependence significantly impairs global cognitive functioning, particularly in domains related to concentration and memory consolidation. Similar findings were reported by Zetsen et al. [19], who demonstrated widespread cognitive impairments in long-term users, especially in processing speed, sustained attention, and executive functioning, even after adjusting for age and education.

Regarding the distribution of high scores across BENDEP domains, problematic use and preoccupation were most frequently observed in individuals with moderate dependence, highlighting a stage where individuals

may still retain cognitive awareness of their misuse but are unable to exert control. This pattern mirrors observations from Kan et al. [20], who emphasized that preoccupation and compulsive behaviors often intensify before overt cognitive decline sets in. Interestingly, the severe dependence group showed fewer high domain scores, possibly reflecting greater cognitive decline or loss of insight, a phenomenon also observed in studies of chronic substance dependence and executive dysfunction [21].

The sociodemographic characteristics of participants offer valuable insight into populations most vulnerable to benzodiazepine dependence. A majority were male (60%), and males were more likely to exhibit moderate or severe dependence. This is consistent with findings from Gallacher et al. [22], who noted that male users often display higher misuse potential, possibly due to differences in prescription patterns, help-seeking behaviors, and stress coping strategies. The most common age group was 36–39 years (49.2%), a period often associated with occupational and familial stress, which may lead individuals to self-medicate with benzodiazepines, as reported by Verdoux et al. [23].

Participants predominantly belonged to the low socioeconomic group (61.7%), a known risk factor for psychological distress and limited access to mental healthcare, thereby increasing the likelihood of prolonged benzodiazepine use [24]. Additionally, lower educational attainment (with 50.8% having only primary-level education) was significantly associated with higher dependence. This supports the notion that limited health literacy impairs awareness of the long-term risks of benzodiazepines, as also found in the VISAT cohort study by Boeuf-Cazou et al. [25]. A high proportion of participants were married (77.5%), suggesting that caregiving and household responsibilities may contribute to stress and sleep disturbances, prompting benzodiazepine use. However, such obligations may also limit the time or resources needed to seek structured treatment.

Overall, the study demonstrates a significant and clinically meaningful association between benzodiazepine dependence severity and cognitive decline, especially in attention, delayed recall, and overall MoCA scores. These findings emphasize the importance of routine cognitive screening among long-term benzodiazepine users, as well as the need for early interventions, such as gradual tapering and cognitive rehabilitation, to prevent potentially irreversible cognitive damage [26,27].

Despite its important findings, the study has several limitations. First, the cross-sectional design restricts the ability to draw causal inferences between dependence and cognitive decline. Second, the sample size, while larger than in many previous studies, was drawn from a single tertiary care center, limiting generalizability. Third, reliance on self-reported measures via the BENDEP-SRQ may introduce recall and social desirability bias, as noted by Kan et al. [20]. Additionally, the study did not account for the duration, dosage, or type of benzodiazepines, all of which can significantly affect cognitive outcomes [17]. Finally, confounding variables such as comorbid psychiatric illnesses, alcohol or other substance use, and concurrent medications were not controlled, possibly influencing both dependence and cognitive performance.

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