



# Prevalence and Predictors of Neurocognitive Impairment, Fatigue, and Health-related Quality of Life in Patients with HIV/AIDS

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## ABSTRACT

**Background:** People living with human immunodeficiency virus (PLHIV) are known to have decreased quality of life (QoL), increased fatigue, and neurocognitive dysfunction. In India, the prevalence and predictors of the same are not explored. We aim to determine the prevalence and predictors of neurocognitive impairment (NCI), fatigue, and health-related QoL among PLHIV in India.

**Setting:** The study was conducted among people attending an antiretroviral therapy center in a tertiary care hospital in New Delhi after ethical approval.

**Materials and methods:** We enrolled consented patients and used the Montreal Cognitive Assessment (MoCA), Multidimensional Assessment of Fatigue (MAF) scale, and 36-item Short Form (SF-36) survey to assess NCI, fatigue, and health-related QoL (HRQoL), respectively.

**Results:** A total of 100 PLHIV with a mean age of  $42.0 \pm 9.6$  years were enrolled, with 48% females. 47 patients (47%) had NCI with a MoCA score  $<26$ . Male gender, PLHIV with  $<5$  years of treatment, and  $<50$  years of age had higher MoCA scores. MoCA scores had a negative correlation with age and MAF scores and a positive correlation with SF-36 scores. 55 patients (55%) suffered from fatigue, with lesser fatigue scores for males. Fatigue scores had a negative correlation with SF-36 scores. 71 patients (71%) had total SF-36 scores  $>50$  with males having higher scores. Fatigue had a negative correlation on QoL,  $r = -0.831$ .

**Conclusion:** In India, the prevalence of NCI, fatigue, and decreased QoL is higher compared to other populations. Management strategies in HIV require interventions to improve NCI, fatigue, and QoL along with antiretroviral therapy.

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## INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is defined by the occurrence of any of the more than 20 life-threatening cancers or "opportunistic infections" due to the immune system weakening. According to the WHO, advanced human immunodeficiency virus (HIV) disease (AHD) is defined as a condition with a CD4 count of  $< 200$  cells/ $\text{mm}^3$  or with the presence of WHO clinical stage 3 or stage 4 disease in the adolescent and adult population. Children  $< 5$  years of age living with HIV infection are also considered as advanced HIV disease.<sup>1</sup> At the end of 2023, 39.9 million and 2.5 million people were living with HIV across the world and in India, respectively. In 2023, an estimated 1.3 million people worldwide were diagnosed with HIV, highlighting the global disease burden. The same year, around 630,000 patients diagnosed with HIV died due to HIV-related causes.<sup>2</sup>

Human immunodeficiency virus has neuroinvasive, neurotrophic, and neurovirulent properties with central nervous system (CNS) infection causing a

myriad of clinical manifestations. However, neurological manifestations in people living with HIV (PLHIV) can result from the direct infection of CNS or opportunistic infections or tumors or due to treatment (side effects and immune reconstitution inflammatory syndrome (IRIS)). Chronic neurodegenerative conditions in PLHIV is referred to as HIV-associated neurocognitive disorders (HAND) with abnormalities in cognitive, behavioral, and motor function. HAND ranges from asymptomatic to minor neurocognitive disorder to HIV-associated dementia (HAD). Although patients with HIV-associated dementia have declined with the advent of highly active antiretroviral therapy (HAART), the prevalence of less severe HIV-associated neurocognitive impairment is rising.<sup>3,4</sup>

Mini-Mental Status Examination (MMSE) and HIV dementia scale are simple bedside cognitive tests used to assess HAD. However, these are inadequate for less severe HIV-associated neurocognitive impairment. MMSE was less sensitive in individuals with a college education and less specific in individuals with less education.<sup>3,5</sup> Montreal Cognitive Assessment (MoCA) is

widely used for assessing neurocognitive impairment (NCI) in PLHIV because of its improved accuracy and low false positive rate.<sup>6</sup>

Health-related quality of life (HRQoL) gives data on the physical and mental health status and the impact of disease on the ability to function in daily life. HRQoL is a good indicator for patients who have chronic illnesses like HIV/AIDS. A greater understanding of the predictors that affect the HRQoL may help identify targets for improving HRQoL in PLHIV. Chronic fatigue is not only highly prevalent among people living with HIV/AIDS, but also one of the most disabling symptoms, significantly impacting the day-to-day functioning of the patient and overall quality of life. In PLHIV, fatigue is strongly linked to psychological factors such as depression, anxiety, and emotional distress.<sup>7,8</sup>

In the Indian context, neurocognitive impairment, HRQoL, and fatigue among PLHIV are not widely explored. We plan to find the prevalence and predictors of fatigue, neurocognitive dysfunction, and HRQoL in PLHIV in India.

## MATERIALS AND METHODS

### Study Design and Site

The study was conducted as a cross-sectional, observational study among all adult PLHIV with age  $> 18$  years on HAART for  $>1$  year under the outpatient department follow-up of the Department of Medicine at our center, a tertiary care teaching hospital in New Delhi, India. Those with a history of opportunistic

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infections within the past 6 months, all cases with a prediagnosed generalized anxiety disorder or depression, any recent demise in the family, or any disease requiring hospitalization in the last year, history of head injury or CNS infection or seizure disorder anytime in the past were excluded.

## Objective

The study was planned to determine the prevalence and predictors of neurocognitive disorders, fatigue, and health-related quality of life (QoL) in PLHIV using the MoCA, Multidimensional Assessment of Fatigue (MAF) scale, and 36-item Short Form Survey (SF-36), respectively.

## Ethical Approval

The study was initiated after ethical approval from the Institute Ethics Committee. Patients were explained about the study using a bilingual participant information sheet, and informed written consent was obtained.

## Sample Size

We calculated the sample size by the expected prevalence of fatigue in PLHIV as 65% based on the results of a previous study,<sup>8</sup> with 10% absolute precision and 90% confidence interval, using a standard online tool.<sup>9</sup> This yielded a sample size of 91 individuals. To adjust for the diversity of opinions, a 10% sample was taken extra, yielding a sample size of 100.

## Data Collection

The data collection instrument consisted of sociodemographic parameters, including gender, age, marital status, level of education, and employment, along with the MoCA test, MAF scale, and SF-36 questionnaire. MAF and SF-36 questionnaires were translated into the local language (Hindi) and were validated before use. A prevalidated Hindi version of the MoCA test was used in the study.

The MoCA test was used to assess the neuropsychological function of PLHIV, and scores less than 26/30 were considered abnormal. The assessment evaluates seven key domains of neurocognitive functions,

namely visuospatial and executive skills, memory including delayed recall, naming ability, language, attention, abstract thinking, and orientation (Table 1).<sup>10</sup> Mild, moderate, and severe cognitive dysfunction were defined by a MoCA score of 18–25, 10–17, and <10, respectively.<sup>11</sup>

Health-related QoL was assessed using the SF-36 questionnaire. The questionnaire consists of 36 items that assess eight domains of health: (1) limitations in physical activities due to health problems, (2) limitations in social activities caused by physical or emotional issues, (3) bodily pain, (4) general mental health—including psychological distress and well-being, (5) restrictions in usual role activities due to physical health, (6) energy and fatigue, (7) limitations in role activities due to emotional problems, and (8) overall perceptions of general health.<sup>12</sup> The eight domains of SF-36 are divided into two groups, physical dominion (comprising of functional capacity, general health status, pain, and physical aspects), to measure the impact of limitations in physical activity of everyday life on HRQoL and the mental health dominion (encompasses multiple areas related to psychological well-being, including mental health, vitality, social functioning, and emotional aspects), analyses the mental health impact. Each domain score was determined, and the global SF-36 score was calculated as the average of the domain scores. Higher SF-36 scores indicate better health status and overall quality of life.<sup>13</sup>

The MAF scale consists of 16 items designed to evaluate four key dimensions of fatigue, namely severity of fatigue, distress, interference of fatigue on daily activities, and timing. Among the 16 items, 14 use a numerical rating scale, while the remaining two are multiple-choice.<sup>14</sup> On evaluation using the MAF scale, patients were asked to reflect on the pattern of fatigue for the past week and also on the effect of fatigue on their day-to-day activities. For every question posed, patients were asked to circle the number from 1 to 10 that most closely indicates how they felt during the past week, with 1 being the least and 10 being the highest

degree. Responses 1 and 2 were considered “nil” fatigue, while responses 9 and 10 were considered “a great deal” of fatigue.

## Statistical Analysis

Data were collected and stored with a Microsoft Excel spreadsheet. Descriptive statistics are presented as mean with standard deviation in continuous variables and median with interquartile range in categorical variables. Non-normally distributed data (confidence scores) were analyzed using the Mann–Whitney test, while normally distributed data were analyzed using Student’s *t*-tests. Correlation among variables was done using the Pearson or Spearman correlation coefficient. The data were analyzed with SPSS software (Version 25.0, Armonk, NY: IBM Corp).

## RESULTS

A total of 100 PLHIV visiting the outpatient department were enrolled. Out of 100, 48% were females. The patients had a mean age of  $42.0 \pm 9.6$  years with an average duration of antiretroviral therapy use of  $4.7 \pm 2.3$  years.

## Neurocognitive Impairment

The mean MoCA score was  $20.4 \pm 5.6$  (68.1%). Males had a significantly higher mean MoCA score ( $27.6 \pm 7.2$ ) than females ( $24.1 \pm 6.8$ ), *p*-value = 0.015. Those with duration of ART <5 years had significantly higher mean MoCA score,  $27.4 \pm 7.0$ , compared to those with duration of ART >5 years,  $24.3 \pm 7.1$ , *p*-value = 0.028. The age of the patient affected the MoCA score significantly, with patients with age >50 years having a mean MoCA score of  $19.7 \pm 6.4$ , and those with age <50 years had a mean MoCA score of  $27.2 \pm 6.7$ , *p*-value < 0.01.

Among the different domains of MoCA, the language domain was the most affected in PLHIV, with a 42.3% decrease, followed by memory and delayed recall, which decreased by 40.6%. Similarly, orientation was the least affected domain among PLHIV with a 14.2% decrease. Table 1 shows the different domains of the MoCA test with the maximum score achievable in each domain and the mean score of patients in each domain.

**Table 1:** Domain-wise mean and maximum achievable MoCA score of PLHIV

Domain	Maximum score achievable	Mean score of the patients	Mean percentage score
Visuospatial/executive	5	$3.17 \pm 1.24$	63.4
Naming animals	3	$2.45 \pm 0.74$	81.7
Attention	6	$3.72 \pm 1.38$	62.0
Language	3	$1.73 \pm 0.78$	57.7
Abstraction	2	$1.25 \pm 0.82$	62.5
Memory and delayed recall	5	$2.97 \pm 1.13$	59.4
Orientation	6	$5.15 \pm 0.99$	85.8

A total of 47 patients (47%) had cognitive impairment (MoCA score <26), with 35, 11, and 1 PLHIV having mild, moderate, and severe cognitive impairment, respectively. PLHIV

with normal MoCA scores ( $n = 53$ ) had higher SF-36 scores (mean =  $70.8 \pm 21.9$ ) than those with cognitive dysfunction ( $n = 47$ ) (mean =  $54.2 \pm 33.3$ ),  $p$ -value < 0.01. People with MoCA

scores  $\geq 26$  had a mean MAF score of  $14.2 \pm 15.7$ , significantly lower than the mean MAF score ( $21.4 \pm 18.9$ ) of those with MoCA scores < 26 ( $p$ -value = 0.04). MoCA scores have a significant negative correlation with the age of patients ( $r = -0.433$ ,  $p$ -value < 0.0001). Similarly, MoCA scores have a significant negative correlation with the MAF scores ( $r = -0.337$ ,  $p$ -value = 0.001). MoCA scores significantly correlated with SF-36 scores and its mental health domain,  $r = 0.451$ ,  $p$ -value < 0.0001, and  $r = 0.476$ ,  $p$ -value < 0.0001, respectively.

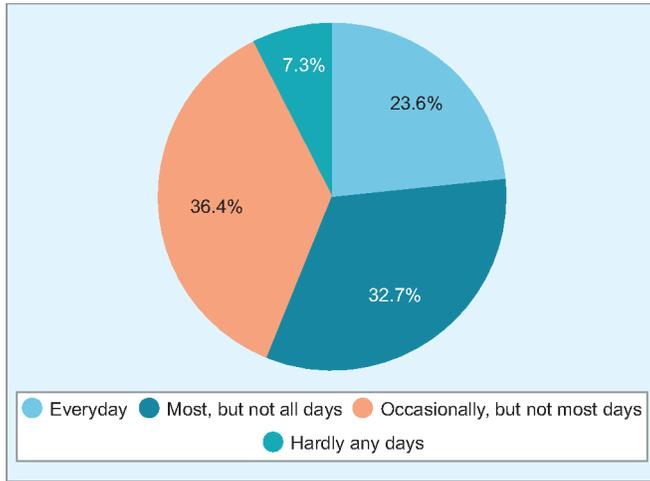


Fig. 1: Pie chart showing the responses of patients on the MAF questionnaire for fatigue

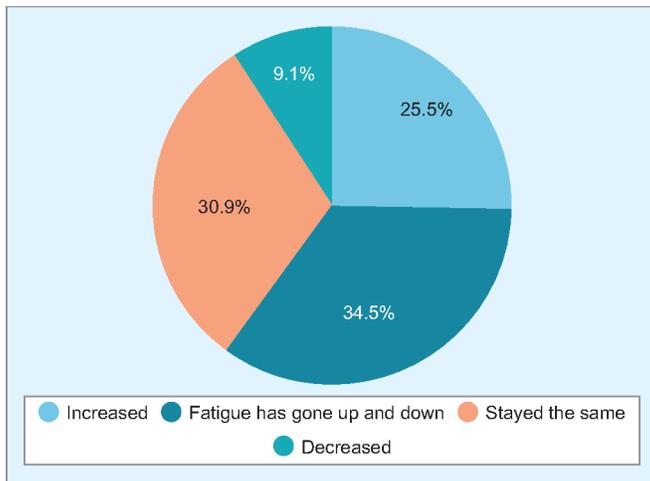


Fig. 2: Pie chart showing the change in the severity of fatigue in the last week

**Fatigue**

Out of 100 patients, 55 patients (55%) reported suffering from fatigue in the past week. The mean MAF score among fatigued patients was  $31.9 \pm 10.1$ . Out of the 55 patients who reported having suffered fatigue in the past week, 13 (23.6%) reported that they suffered fatigue daily, and four reported that they had fatigue on hardly any days in the past week (Fig. 1). Of the 55 patients who reported having suffered fatigue, 14 (25.5%) reported that their fatigue increased during the last week, fatigue went up and down in 19 patients (34.5%), stayed the same in 17 (30.9%), while it decreased in 5 (9.1%) (Fig. 2). Among different aspects of fatigue, “exercise other than walking and engaging in sexual activity” was the most opted aspect, 32.7% ( $n = 18$ ) and “dress” was the least opted aspect, 5.4% ( $n = 3$ ) (Table 2).

Males reported a significantly lower (mean =  $11 \pm 14.1$ ) MAF score compared to females (mean =  $24.5 \pm 18.5$ ),  $p$ -value < 0.01. MAF scores were unaffected by the patient’s age and duration of ART. There were no significant differences in the MoCA scores of the patients who reported fatigue and those who did not. The mean SF-36 scores

Table 2: Different ratings for each question given by the patients who are suffering from fatigue, calculated with the MAF questionnaire

Questions asked	The mean degree of fatigue in that aspect ( $n = 55$ )	Percentage of patients who reported “a great deal” in that aspect ( $n = 55$ )
To what degree have you experienced fatigue	$6.16 \pm 2.28$	12.7
How severe is the fatigue that you have been experiencing	$6.29 \pm 2.08$	9.0
To what degree has fatigue caused you distress	$6.65 \pm 2.41$	10.9
Do household chores	$5.49 \pm 2.37$	7.3
Cook	$4.56 \pm 3.08$	7.3
Bath or wash	$4.07 \pm 2.67$	7.3
Dress	$3.44 \pm 2.84$	5.5
Work	$6.58 \pm 2.28$	10.9
Visit or socialize with friends or family	$6.44 \pm 2.67$	12.7
Engage in sexual activity	$7.62 \pm 2.49$	32.7
Engage in leisure activities	$6.62 \pm 2.44$	14.5
Shop and do errands	$6.76 \pm 2.25$	14.5
Walk	$6.40 \pm 2.30$	9.0
Exercise other than walking	$8.18 \pm 1.91$	32.7

**Table 3:** Descriptive analysis of eight different domains of the SF-36 questionnaire

Domains of health-related quality of life	Mean $\pm$ standard deviation (n = 100)
Physical health problems	67.15 $\pm$ 33
Emotional health problems	62.09 $\pm$ 25.79
Social activities	65.38 $\pm$ 25.92
Pain	66.00 $\pm$ 29.04
Role limitations due to physical health problems	65.25 $\pm$ 45.07
Role limitations due to personal or emotional problems	69.00 $\pm$ 44.76
Energy/fatigue	57.20 $\pm$ 26.45
General health perceptions	51.95 $\pm$ 27.14

were significantly higher in people with no fatigue (mean = 83.5  $\pm$  14.3) than in those who reported fatigue (mean = 46.2  $\pm$  27.0) ( $p$ -value < 0.01). Fatigue scores had a strong negative correlation with SF-36 scores and its physical and mental health domains,  $r = -0.831$ ,  $p$ -value < 0.0001,  $r = -0.84$ ,  $p < 0.0001$ , and  $r = -0.795$ ,  $p$ -value < 0.0001, respectively.

### Health-related Quality of Life

The overall mean global SF-36 score was 63.0  $\pm$  28.9. The mean global SF-36 score was significantly higher in males (74.1  $\pm$  23.4) compared to females (50.9  $\pm$  29.6),  $p < 0.01$ . However, the mean SF-36 scores were unaffected by age and duration of the ART. A total of 71 patients had total SF-36 scores >50. Patients with SF-36 score >50 had higher MoCA scores (mean = 27.8  $\pm$  6.5) than those with SF-36 <50 (mean = 21.2  $\pm$  6.7,  $p$ -value < 0.01). Patients with SF-36 scores >50 had significantly lower MAF scores (mean = 9.9  $\pm$  12.8) compared to those with SF-36 scores <50 (mean = 37.6  $\pm$  10.1,  $p$ -value < 0.01). The physical health domain was more affected compared to mental health, with a mean score in the mental health domain of 82.5  $\pm$  34.4 and 77.0  $\pm$  35.8 in the physical health domain.

Among different domains of SF-36, general health perceptions were the most affected in PLHIV, with a mean score of 51.9  $\pm$  27.1, and "role limitations due to personal or emotional problems" were the least affected (mean = 69.0  $\pm$  44.7) (Table 3). 13 (13%) patients reported better general health compared to their health 1 year ago, while eight (8%) reported worsened general health.

Twenty-five (25%) of patients reported facing no bodily pain in the past 4 weeks, while 5% reported facing very severe bodily pain. A total of 31 patients (31%) reported that the emotional problems had no impact on their routine social interactions with the family, friends, neighbors, or community groups. Ten and three patients reported that emotional problems caused very severe and severe interference in their normal social activities with family, friends, neighbors, or groups, respectively. Out of the 100 patients,

25% felt that their physical health or emotional problems had no impact on their social activities, while 4% of the patients reported that it interfered with their social activities all of the time.

### DISCUSSION

In this hospital-based cross-sectional study, we explored the prevalence of neurocognitive dysfunction, quality of life, and fatigue in PLHIV on ART for more than 1 year. In the Indian population, the prevalence and factors affecting the former were not explored. With the reduced mortality largely due to the widespread use of HAART, the QoL and its factors gain more importance. We report the higher prevalence of fatigue and neurocognitive dysfunction in PLHIV and the urgent need to improve their QoL.

The Montreal Cognitive Assessment is a widely used and accepted tool for assessing NCI. In our study, the prevalence of neurocognitive dysfunction was 47%. Studies from India reported lesser MCI among the Indian population: In diabetic patients, the prevalence of NCI was 35.6% with a median age of 58 years,<sup>15</sup> while in the normal population, the NCI was 58% with a median age of 70 years.<sup>15</sup> Compared with these, the prevalence of NCI is very high in PLHIV, especially with 42 years as the mean age for NCI in PLHIV. Various studies have shown a higher prevalence of NCI among PLHIV.<sup>15</sup> The mean MoCA score was lesser compared with other studies in PLHIV. There was a significant gender difference in MoCA scores in our study, probably due to the differences in mental health, hormonal, and genetic differences between males and females.<sup>16</sup> NCI was found to increase significantly with increasing duration of ART. However, longer disease duration is associated with a rise in the incidence of HAND.<sup>15</sup> The increased prevalence of NCI may indicate that newer strategies need to be devised to prevent HAND in patients who have been infected for a long duration apart from ART.

Neurocognitive impairment has an independent association with depressed mood, and in our study, MoCA scores had a significant positive correlation with the mental health domain of SF-36.<sup>15</sup> Cognitive dysfunction was also associated with increased severity of fatigue. NCI had a significant negative correlation with fatigue, and NCI can be one of the factors for fatigue among PLHIV; vice versa may not be true. In people with poor HRQoL, cognitive dysfunction and fatigue were found to be significantly increased, which indicates that QoL has a positive impact on physical, mental, and cognitive health. PLHIV with cognitive dysfunction had a poor quality of life, with a significant positive correlation, warranting strategies that reduce cognitive dysfunction to improve HRQoL.

Fatigue is among the most prevalent and distressing symptoms experienced by individuals living with HIV, with reported prevalence rates ranging from 33 to 88%.<sup>17</sup> Gender has a significant effect on fatigue, with females having higher fatigue scores. In the Indian population, this could be attributed to hormonal changes, iron deficiency, lifestyle, lack of self-care, poor quality of sleep, and psychological stress.<sup>18</sup> The result, however, indicates the need for better preventive strategies oriented toward females. The duration of ART did not affect MAF scores, indicating that PLHIV may face fatigue even during initial phases of diagnosis and treatment. The QoL is better among nonfatigued patients, indicating that the interventions targeting fatigue in the Indian population can significantly improve the QoL of patients with HIV infection. With the reports of fatigue due to ART can potentially interfere with treatment adherence; measures to target fatigue can help in improving treatment adherence.<sup>19</sup> People with fatigue did not have a significant increase in NCI, indicating that the cognitive dysfunction may have caused fatigue; the vice-versa may not hold.

The mean SF-36 score in our study was lower than that measured for the normal Indian population and also lower compared to other populations affected with HIV.<sup>20</sup> This decline in QoL could be attributed to the struggles associated with PLHIV, differences in the perceptions of a good QoL, and the nonavailability of a social support system in India for PLHIV.<sup>21</sup> Males have higher SF-36 scores as reported by other studies in the past.<sup>21</sup> This could be because females are physiologically more prone to emotional and physical stress and they have lesser family and institutional support compared to males in India.<sup>10,22</sup>

The duration of ART taken did not affect HRQoL in our study. Similar studies from Pakistan and Kenya found that the

time since diagnosis of HIV infection and the duration of ART negatively affected HRQoL, respectively, while a similar study from India found the same was better in people taking ART for a longer duration.<sup>23–25</sup> These differences may be because of the differences in the perceptions of subjective indices like QoL.

This study paves the way for exploring deeper into the issues of increased fatigue, NCI, and decreased QoL among PLHIV in India. This also asserts the need for a more proactive and dynamic social support system for PLHIV in India, and also key interventions focusing not just on medically managing HIV infection and opportunistic infections, but comprehensively intervening in the patients as a whole. A qualitative study focusing on what patients need can help in guiding the interventions as per the needs of the population. More studies focusing on patient-reported outcomes are warranted in India. Routine use of these patient-reported outcomes with medical care in ART centers can improve adherence and overall life of PLHIV in India.

This study has potential limitations. The data were collected in a single interview with the patients and could not be compared with baseline deficits in HRQoL, neurocognitive dysfunction, and fatigue present in the patients before HIV infection. The limitation is common in similar studies, especially in resource-limited settings. The influence of the disease severity, opportunistic infections, and the effect of polypharmacy is not known from this study. Being a single-center study from a tertiary hospital in New Delhi, the results may not be generalizable to the broader Indian population, especially those from rural settings or managed at primary-level facilities. However, single-center studies remain valuable for hypothesis generation and baseline data collection in under-researched contexts. The cross-sectional study design is unable to establish causal relationships between NCI, fatigue, and HRQoL; nonetheless, the strength and direction of the correlations provide a rationale for future longitudinal research. Fatigue and HRQoL were self-reported in our study, which may have introduced a potential recall bias. Selection bias may also have occurred because all participants were on ART for >1 year; thus, early-stage or ART-naïve patients were not included. This was intentional to reduce confounding by acute illness, but may underestimate variability in earlier disease stages. Though the MoCA <26 cut-off is internationally accepted, it may be influenced by cultural and educational

factors in the Indian context; future studies should validate local thresholds. Also, the predictors were assessed mainly through correlation and bivariate analyses; multivariate regression could have been better controlled for confounding. This was limited by the modest sample size, but it will be prioritized in follow-up studies. ART regimen-specific effects on fatigue and NCI were not examined in our study; incorporating regimen type, duration, and side effects may yield more targeted clinical recommendations. Qualitative data exploring patient perspectives were not collected; integrating such insights into future mixed-method studies could enrich understanding and guide patient-centered interventions.

Despite these limitations, our study contributes novel data on the burden and correlates of NCI, fatigue, and HRQoL among Indian PLHIV—a population in which such relationships are underexplored. The findings underscore the need for multicenter, longitudinal, and mixed-method research to develop targeted interventions, as well as integrating neurocognitive and psychosocial screening into routine HIV care in India.

## INFORMATION ON PREVIOUS PRESENTATION/PUBLICATION

NA.

## SOURCE OF SUPPORT

No funding was required.

## CONFLICTS OF INTEREST

The authors have no conflicts of interest.

## USE OF ARTIFICIAL INTELLIGENCE

Artificial intelligence was not used.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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