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The Effects of Anti-Retroviral Therapy on Cognition and Psycho-Motor Performance of Patients with HIV Positive Status and its Association with Medication Adherence

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Abstract

Background: The introduction of anti-retroviral therapy (ART) has had a strong impact on morbidity and mortality, including a decrease in the prevalence of the most severe forms of HIV-associated neurocognitive disorders (HAND). Even in its mildest form, HAND can negatively impact ART adherence, quality of life, ability to perform activities of daily living, and working capacity. Increasing evidence describes cognitive performance as a changeable condition, suggesting fluctuations and possible decline may occur over time. Studies have assessed cognitive performance in cohorts receiving ART and observed associations highlighting vulnerable sub-populations. The number of studies addressing cognitive performance in resource-limited countries has increased over the last decade. However, there is a paucity of studies correlating the effect of ART on cognition and psycho-motor performance with positive medication adherence. This study was therefore designed to assess cognitive impairment using the MoCA test (Montreal Cognitive Assessment) and its association with ART adherence and CD4 count, and the utility of the MoCA test as a tool to detect cognitive decline over a period in HIV positive patients.

Methods: A 30-point MoCA test was conducted in 150 HIV positive patients.

Results: In the present study, significant cognitive impairment (MoCA score <26) was found in HIV positive patients with CD4 count < 200 cells/ml & a resounding majority of the HIV positive patients also showed cognitive impairment, with a greater preponderance towards the uneducated subjects and those with medication non-adherence.

Conclusions: The HIV positive patients with higher CD4 count and good ART adherence have a lower incidence of cognitive impairment over a period. The MoCA test could be used as an early detection tool for ART non-adherence and disease progression in patients with cognitive decline.

Keywords

MoCA; ART adherence; Cognitive decline.

Introduction

Early in the infection process, HIV may enter the central nervous system (CNS) and spread swiftly throughout the brain parenchyma [1]. As the illness worsens, HIV-related cognitive symptoms become more noticeable [2,3]. The introduction of anti-retroviral therapy (ART) has had a strong impact on morbidity and mortality, including a decreasing prevalence of the most severe forms of HIV associated neurocognitive disorders (HAND). Even in its mildest form, HAND can negatively impact ART adherence, quality of life, ability to perform activities of daily living and working capacity [1-3]. Increasing evidence describes cognitive performance as a changeable condition suggesting fluctuations, and possible decline may occur over time [4]. Research indicates that anti-retroviral therapy is linked to steady or enhanced cognitive performance [4,5]. Studies have assessed cognitive performance in cohorts receiving ART and observed associations highlighting vulnerable sub-populations [5,6]. The number of studies addressing cognitive performance in resource-limited countries has increased over the last decade. However, whether potential long-term low levels of CNS exposure to HIV in people with suppressed peripheral blood HIV levels ultimately lead to CNS alterations such neurocognitive impairment is yet unknown. There is paucity of studies correlating the effect of ART on cognition and psycho-motor performance with positive medication adherence, which is addressed by this study.

Materials and Methods

After taking Institutional Ethics Committee approval (SKNMC/Ethics/App/2022/985), this cross-sectional study was carried out for 6 months at ART-center of a tertiary care hospital in India. Written Informed Consent of the subjects was taken. One hundred fifty adults' patients of either sex with positive HIV status, and following ART regime for more than 12 months without any prior mental illness were included in the study. Socio-demographic characters like age, gender, education, habits were recorded. The latest reports of the patient containing their CD4 counts were obtained and noted to assess the disease progression. A normal CD4 count is generally considered to be between 500 and 1500 cells/ml. A CD4 count below 200 cells/ml is a key criterion for diagnosing AIDS.

The MoCA a standardized and rapid tool to assess cognitive abilities, was given to the patients and score was assessed at once. The MoCA test [maximum score: 30 points] in which points were allotted for the

following abilities: (i)Visuospatial/Executive [0-5 points] (ii)I dentification [0-3 points] (iii) Memory [no points] (iv)Attention [0-6 points] (v) Language [0-3 points] (vi)Abstraction [0-2 points] (vii)Delayed recall [0-5 points] (viii) Orientation [0-6 points]. Cognitive Impairment was defined as MoCA score < 26 [7].

A structured proforma comprising of 10 questions was used to determine the drug adherence of selected candidates. The first six questions (Q1-6) & Q9, Q10 are scored "NO=1 & YES=0". While Q7 & Q8 are scored as "NO=0 & YES=1". The score reflects the degree of compliance-compliant if the score is higher than non-compliant if the score is low. [i.e patients are compliant if they respond "NO" to (Q1-6) & Q9, Q10; and "YES" to Q7 & Q8]. A score of 10 is considered adherent and less than 10 indicates non-adherent [4].

Data was collected in MS Excel sheet and analyzed using analysis of variance (ANOVA) followed by post hoc Tukey's statistical test and chi-square test for association of the MoCA score with medication adherence and CD4 count in HIV positive patients, (non-parametric tests) using the OpenEpi, version 2.3 (Andrew G. Dean and Kevin M. Sullivan, Atlanta, GA, USA) and online VassarStats: Website for Statistical Computation, (Richard Lowry, USA), respectively. $p < 0.05$ was considered significant.

Results

Table 1 and Table 2 presents the socio-demographics and medication adherence of 150 study participants. The mean age of participants was 54.87+0.8 and 50.72+0.5 in patients with positive adherence and negative adherence respectively; 81 were males and 69 females. Among the 150 participants, only 36 held a postgraduate degree. Based on CD4 levels, progression of disease was controlled in two-third of the patients (CD4>200). Additionally, over half of the sample had been living with HIV for at least 10 years. This progression was found more in patients with negative adherence.

Demographics	**Study Group**	
	Patients with positive adherence	**Patients with negative adherence**
Mean Age	54.87	50.72
Age group		
20-30 years	21	15
30-40 years	30	18
40-50 years	35	10
50-60 years	10	11
Gender		
Male	53	28
Female	43	26
Education		
Non-graduate	33	24
Graduate	42	15
Postgraduate	21	15
Habits		

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Smoking	6	3
Tobacco	55	6
Alcoholic	3	0
Nil	72	45
Diet		
Vegetarian	30	27
Non-vegetarian	3	3
Mixed	63	24
CD4 count		
<200	28	38
>200	68	16

Table 1: Socio-demographics of participants in the study groups (N=150).

No	Question	Yes N (%)	No N (%)
1.	Do you ever forget to take your medication?	54 (26)	111 (74)
2.	Are you careless at times about taking your medication?	62 (41.3)	88 (58.7)
3.	When you feel better, do you sometimes stop taking your medication?	57 (38)	93 (62)
4.	Sometimes if you feel worse when you take the medication, do you stop taking it?	68 (45.3)	82 (54.7)
5.	I take my medication only when I am sick	32 (21.3)	118 (78.7)
6.	It is unnatural for my mind and body to be controlled by medication	66 (44)	84 (56)
7.	My thoughts are clearer on medication	98 (65.3)	52 (34.7)
8.	By staying on medication, I can prevent getting sick	112 (74.7)	38 (25.3)
9.	I feel weird on medication	57 (38)	93 (62)
10.	Medication makes me feel tired and sluggish	59 (39.3)	91 (60.7)

Table 2: Medication Adherence Rating Scale (MARS) questionnaire results (N=150).

The mean total cognitive score showed a clear and significant association with adherence and CD4 count suggestive of evident cognitive impairment (p=0.017). This relationship is consistent across the mean scores of the seven sub-domains but was statistically significant in the visuospatial/executive (p=0.003), Naming (p=0.021), Delayed Recall (p=0.033) and Orientation domain (p=0.043) respectively. (Table 3).

Cognitive Domain	Highest score	Patients with positive adherence Mean Score (SD)	Patients with negative adherence Mean Score (SD)	Patients with CD4 Count <200 cells/ml Mean Score (SD)	p- Value
Total Score on MoCA	30	24.9±3.7	21.9±4	21±1.7	0.017*
Visuospatial/Executive Function	5	3.42±1.7	2.95±1.7	2.54±1.2	0.003*
Naming	3	2.88±0.7	2.13±0.4	1.95±0.2	0.021*
Attention	6	4.87±1.5	4.33±1.2	3.67±1.3	0.423
Language	3	2.65±1.2	2.00±0.8	1.92±0.9	0.083
Abstraction	2	02.00±0	02.00±0	02.0±0	0.262
Delayed Recall	5	2.85±1.5	2.16±1.2	1.89±1.7	0.033*
Orientation	6	5.73±0.7	5.32±0.6	5.25±1.2	0.043*

Table 3: Mean MoCA score in HIV patients on ART for total cognitive function and each subdomain (N=150).

*p<0.05, p Values by analysis of variance (ANOVA) followed by post *hoc* Tukey's statistical test.

When association between cognitive impairment and CD4 count in ART non-adherent patients was studied, by Fisher exact probability test with Freeman-Halton extension, we found significant association between them; p=0.021494 (Table 4). We also studied association between cognitive impairment and adherence by chi-square non-parametric test; Table 5 shows that there was significant association (p= 0.02301).

MoCA Score	No. of Patients	No of non-adherent patients Mean (SD)	No of patients with CD4 count <200 cells/ml	p Value
0-25	110	29 (2.2)	48	0.021494
Above 26	40	25 (2.3)	18	

Table 4: Association of the MoCA score with CD4 count in ART non-adherent patients.

p Value by Fisher exact probability test with Freeman-Halton extension.

MoCA Score	No. of Patients	Mean score (SD)	p Value
0-25	84	23.06 (1.48)	0.02301
Above 26	12	28 (1.87)	

Table 5: Association of the MoCA score with ART adherence in HIV patients.

p Value by chi-square non-parametric test.

Discussion

The MoCA is a commonly used instrument for evaluating cognitive impairment and is mainly used to identify patients who may be experiencing cognitive decline [7]. The MoCA scale was employed in this study to evaluate the cognitive function of people on ART, with HIV positive status, taking into account

their overall cognitive capacities and performance in a range of cognitive areas. In order to detect any cognitive impairment in them and compare it with the cognitive function of HIV positive persons with and without medication adherence and CD4 count (disease progression), we used this standardized test to assure consistent and objective assessment of cognitive performance. A MoCA score of 26 or higher is defined as normal cognitive abilities. Present study demonstrated that more than 73% of participants had cognitive impairment (MoCA< 26). A recently performed study in assessing cognitive function among patients on ART with HIV positive status revealed that the patients with low CD4 count and poor medication adherence is associated with increased risk of cognitive dysfunction [8]. These results are in agreement with our study results which are evident with lower mean total cognitive score showed a clear and significant association with adherence and CD4 count (p=0.017). This relationship found consistent across the mean scores of the four of seven sub-domains, and statistically significant in the visuospatial/executive (p=0.003), Naming (p=0.021), Delayed Recall (p=0.033) and Orientation domain (p=0.043) respectively.

Few studies however mention variable results when the association between ART adherence and cognitive decline was studied, these studies mention cognitive decline have negative impact on adherence and vice a versa as the disease progress [9]. These studies however carried out in patients above 60yrs wherein, our study population was between 18-60yrs. In elderly patients it becomes difficult to understand whether cognitive decline is due to age related neurodegeneration or non-adherence and disease progress. Results of our study thus add valuable piece of information on the association between ART adherence, disease progression (CD4 count) and cognitive decline as we have included young HIV positive patients.

Effective ART has lessened the severity but not the frequency of cognitive impairments. A study by Alford et al. mentions impairments in executive function that affect working memory, attention and prospective memory, or the ability to 'remember to remember'. The impact of all this is a reduction in quality of life, lower levels of medication adherence, which may jeopardize both the long-term effectiveness of treatment for the individual and increase risk of onward transmission [10]. We also found strong association between cognitive decline, ART adherence and progression of disease.

When association between cognitive impairment and medication adherence was studied there, we found significant association (p= 0.02301), suggestive of delay in disease progression in medication adherent patients which had positive impact on cognitive functions as evident on MoCA. These results are in accordance with earlier few studies mentioning this positive association [11,12].

It is crucial to determine which cognitive domains are most impacted in HIV positive patients on ART; adherent and/or non-adherent in order to target risk modification. This may involve effective ART and implementing cognitive rehabilitation therapies, such as exercise and physical activity, which are necessary to improve executive functioning and lower the risk of cognitive impairment. MoCA test can be useful tool in early detection of ART adherence in HIV positive patients preventing cognitive decline as changes in the brain due to initial infection (viremia) can be rectified by effective ART reducing initial viral load and exposure to brain [8].

Conclusion

This study demonstrated that HIV positive patients' non-adherent to medication do suffer from significant cognitive impairment, then ART adherent patients and patient with lower CD4 count (< 200 cells/ml) are at more risk of developing cognitive impairment. Measures must be taken to improve medication adherence and hence the disease progress, in order to prevent cognitive decline and MoCA test can be a useful tool in detection of cognitive decline associated with adherence and the disease progress in HIV positive patients.

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