RESEARCH

INFLUENCE OF HIV ON NEUROCOGNITIVE PERFORMANCE AND THE ROLE OF CD4 COUNT IN COGNITIVE IMPAIRMENT

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Abstract

Background: It is generally established that HIV penetrates the central nervous system (CNS) early in the infection process and that up to 50% of HIV-infected people develop neurocognitive impairment. The low CD4 cell count and advanced age were shown to be risk factors for HIV-associated cognitive disease. As a result, the current research was conducted to investigate the effects of neuropsychological performance in HIV-positive individuals. **Materials and Methods:** The study was performed at the ART-Centre, Govt. Rajaji hospital, Madurai, Chennai, from Jan. 2008 to Sept. 2008. A total of 60 patients were enrolled on the study, with 30 index subjects having a CD-4 count of less than 250 cells and 30 control subjects having a CD-4 count of more than 250 cells. All the patients were screened for socio-demographic and illness-related variables. They were evaluated for psychiatric, neurological, and neuro-psychological performance. Then ARVT with three medicines (Lamivudine, Zidovudine, and Nevirapine) was added to the index cases. The follow-up of all patients was carried out on both groups after 3 months. **Result:** In comparison to controls, the index patients had severely impaired cognitive functions, according to the findings of this research. Our research found significant impairment in both sustained and focused attention. In terms of mental speed, motor speed, and memory, no significant differences were found. There is no link between CD-4 count and cognitive scores. **Conclusion:** The current study shows that early detection and treatment of cognitive impairment by including a psychiatrist as a team member in ARVT or requiring the psychiatrist's opinion for all HIV positive patients may lead to better results. More research needs to be done to figure out what HIV causes cognitive problems and how they affect daily life and work.

INTRODUCTION

AIDS has been documented in virtually every nation on the planet, making HIV infection a worldwide epidemic. Human immunodeficiency virus type 1 (HIV-1) infection may have serious consequences for the CNS and immune system. HIV-related neuropsychiatric illnesses may be primary or secondary.[1] HIV-related dementia and mild cognitive dysfunction are examples of primary consequences that may be linked to the virus's infection of the central nervous system. Immune suppression may result in a range of brain-related problems, such as opportunistic infections and malignancies and acute and sub-acute disorders.[2] According to research, HIV-associated cognitive disease (HACD) incidence varies depending on the viral clade. In Uganda, for example, clades A and D are the most common sub-types, and research indicated that 31% of HIV-positive people had dementia and 47% had moderate cognitive impairment.[1,2] In another Ugandan investigation, a low CD4 cell count and advanced age were shown to be risk factors for HACD. In contrast, research in Ethiopia, which is largely clade C, found no cognitive impairment in HIV-positive people

compared to control people on a dementia screening test.[3,4] Mild to moderate cognitive impairment was found in 60.5% of clade C HIV+ patients in southern India, but there was no functional impairment that could be seen by a doctor. Similarly, Chinese research found that 34.2 percent of HIV+ people had cognitive impairment, with 39.7% of those who have HIV and hepatitis-C virus co-infection having cognitive impairment.[5] Recently, research in South Africa, which is likewise largely clade C, discovered that HIV+ individuals starting antiretroviral medication had a frequency of 42.4 percent of moderate cognitive dysfunction and 25.4 of percent dementia. A lower level of education, advanced age, and being a male were all risk factors.[6,7]

While ARVT has had a significant impact on the frequency and extent of HAND, the mild variant still exists. This might be due to various reasons, including the late start of ARVT, limited CNS penetration of a number of ARVs, the resistance of drugs, possible neurotoxicity of ARV, improper adherence to medication, long-term HAART adverse effects such as cardiovascular illness, and chronic HIV-brain infection.[8,9]

Diagnosis of HACD is critical, not only clinically but also to guarantee that vital medical resources are allocated properly in the area worst hit by the HIV pandemic.

To address this, the following objectives guided the current study:

1) To determine cognitive impairment among HIV-positive people
2) To determine the pattern or kind of cognitive impairment in HIV-positive patients.
3) To investigate the relationship between CD4 count and cognitive impairment.

MATERIALS AND METHODS

Govt. Rajaji Hospital's Institute Ethical Committee approved the methodology of the present study. From January to September 2008, a study was conducted at the ART-Center, Govt. Rajaji Hospital, Madurai, Chennai. Randomization was accomplished by selecting a group of patients who met the following criteria.

Inclusion criteria

The ELISA test is used to diagnose seropositive individuals. Patients should be between the ages of 18 years to 50 years of age and be able to read and write. To attend the interview, the patient must be clinically stable. Those who agreed to participate in the first research and subsequent follow-up.

Exclusion criteria

Subjects should not be suffering from any mental disease, including substance-induced disorders, either now or in the past. There should be no current or previous neurological diseases or a history of head injuries in the patient. There should be no sensory-motor impairment in the subjects. Patients with a serious medical condition or a long-term pharmacological regimen would make it impossible to complete the study.

Operational Methods

The patients for the research were identified by an ICTC medical officer based on HIV positive by ELISA, and after that, the author chose the individuals at random depending on inclusion criteria. After determining the patient's suitability for neuropsychiatric interview, the subject was informed of the study's purpose. The secrecy of the information was guaranteed. Following the patient's assent, the interview was conducted in a single setting or numerous settings as required or at the patient's choice. This facilitated the researcher's ability to conduct a cooperative and trustworthy interview with the patient. Due to the fact that a CD-4 count of 250 cells is considered the cut-off point for initiating ARVT in HIV patients (as observed in our ARVT-center), 30 subjects with a CD-4 count of less than 250 cells were considered as index cases and 30 subjects with a CD-4 count of more than 250 cells were designated as control. All the patients were screened for socio-demographic and illness-related variables, they were evaluated for psychiatric, neurological, and neuro-psychological performance. Then ARVT with three medicines (Lamivudine, Zidovudine, and Nevirapine) was added to the index cases. After three months, both groups were re-evaluated.

Tools used

1. MINI-International Neuro-psychiatric Interview.[10]
2. Standard progressive matrices.[11]
3. Finger tapping test.[12]
4. Digit symbol substitution Test.[13]
5. Color Trails Test.[14]
6. Digit vigilance Test.[15]
7. PGI Memory scale.[16]

Statistical design

The student's t-test was utilized to evaluate mean values across groups, and the paired t-test was utilized to compare variables within each group over the follow-up period. Pearson's coefficient of correlation was used to determine the significance of the link between predictors and neuropsychological tests. Analysis of covariance (ANCOVA) was used to figure out how important it was that the index group's cognitive skills got worse over three months compared to the controls.

RESULTS

[Table 1] summarizes the demographic variables of control and index group patients. It reveals that around 66 percent (20) of the index patients are

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under the age of 35. Around 53% of participants in control groups are under the age of 35. Both groupings indicate the age group that is most impacted.

Both groups have around 75% male individuals, reflecting the male population's high prevalence and awareness. Rural and urban populations are almost the same (50 percent) in the index groups, but rural populations marginally outnumber urban populations in the control groups.

Around 80% of both categories are married, and around 30% of both groups are self-employed; the remainder work as salaried individuals. The minimum level of education in two groups is the seventh class; around 26% of both groups study beyond the tenth standard.

Table 1: Demographic variables of index and controls group patients

	Index Group (N=30)	Controls (N=30)
Age in years		
21 to 35	20 (66.66%)	16 (53.33%)
35 to 50	10 (33.33%)	14 (46.66%)
Income		
Above Rs 2500	11 (36.66%)	8 (26.66%)
Below Rs 2500	19 (63.33%)	22 (73.33%)
Sex		
Men	23 (76.66%)	22 (73.33%)
Women	7 (23.33%)	8 (26.66%)
Domicile		
Rural	15 (50%)	20 (66.66%)
Urban	15 (50%)	10 (33.33%)
Marital Status		
Married	25 (83.33%)	26 (86.66%)
Single	5 (16.66%)	4 (13.33%)
Occupation		
Salaried	21 (70%)	20 (66.66%)
Self-Employed	9 (30%)	10 (33.33%)
Education		
7 to 10th STD	22 (73.33%)	23 (76.66%)
Above 10th STD	8 (26.66%)	7 (23.33%)

Comparing disease-related factors revealed that the index group had a lesser CD-4 count and a longer period of sickness, the difference was statistically significant [Table 2]. Whereas blood urea and sugar levels were not reported to be statistically significant.

Table 2: Disease-related characteristics of Index and control group patients

	Cases (N-30) Mean (±S.D)	Controls(N-30) MEAN (±S.D)	't'
CD-4 count	190.89 (±79.4)	361.70 (±68.3)	9.45**
Duration in months	16.89 (±12.6)	10.93 (±6.8)	2.71**
Blood UREA	24.33 (±7.7)	25.13 (±5.2)	0.49
Blood sugar	96.03 (±16.3)	98.53 (±14.0)	0.56

Df = 58 ** p < .01

When the index and control groups' neuropsychological performance was compared, statistically significant differences were seen in the color trail tests 1 and 2 as well as the Digit Vigilance-Error score [Table 3]. Index patients reported with lower Raven's matrices and PGI memory scale scores. The length of finger tapping 1 and 2 and digit vigilance-time was greater in index patients than in controls, although the differences were not statistically significant.

Table 3: Neuropsychological performance of index and control group patients.

	Cases (N-30) Mean (SD)	Controls (N-30) Mean (SD)	't'
Raven's Matrices	18.86 (±4.8)	20.13 (±4.7)	1.65
Finger Tapping			
Right	29.70 (±3.3)	28.80 (±2.7)	1.37
Left	29.00 (±3.5)	27.60 (±2.3)	1.91
Digit Symbol test	7.76 (±2.9)	5.43 (±1.8)	1.44
Color Trail			
1	4.10 (±1.5)	3.16 (±0.6)	3.24**
2	7.20 (±2.1)	5.96 (±1.2)	2.90**
Digit Vigilance			
Time	4.33 (±1.1)	3.83 (±1.3)	1.66
Error	1.16 (±1.5)	0.50 (±0.7)	2.36*
PGI Memory Scale	75.43 (±9.6)	79.00 (±7.2)	1.72

Df = 58. * p < .05; ** p < .01.

Correlations between neuropsychological performance and disease-related factors were investigated, and it was discovered that digit vigilance-time was substantially linked with age, but the other correlations were reported to be statistically insignificant [Table 4].

Table 4: Correlation between disease factors and cognitive performance in index patient's

	Age	Duration	CD-4
Raven's Matrices	0.04	0.26	-0.05
Finger Tapping			
Right	0.11	-0.13	0.13
Left	0.12	-0.14	0.18
Digit symbol	0.27	-0.06	-0.21
Color Trail test			
One	0.25	0.04	-0.28
Two	0.31	0.03	-0.24
Digit Vigilance			
Time	0.42**	-0.31	-0.19
Error	-0.08	0.02	-0.14
PGI Memory Scale	-0.21	0.07	0.31

Reading denoted Pearson's γ.

* p < 0.05; ** p < 0.01.

Reading denoted as * are statistically-significant.

During the first and follow-up visits, the neuropsychological performance scores of control patients were compared (after 3 months). It revealed that although Raven's matrices and PGI memory scale scores changed somewhat, they were not statistically significant. The results of the digit vigilance and digit symbol substitution tests showed almost little improvement [Table 5].

Over the course of three months, the neuropsychological functions of the index and control groups were compared, and it was discovered that none of the factors were significant [Table 6].

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Table 5: During the first and follow-up visits (after 3 months), the neuropsychological performance scores of control patients.

	Controls (N-30) Mean (SD)	Follow-up (N-30) Mean(SD)	Paired ' t'
Raven's Matrices	20.13 (±4.7)	20.37 (±4.3)	0.74
Finger tapping			
Right	28.80 (±2.7)	28.70 (±2.7)	1.13
Left	27.60 (±2.3)	27.67 (±2.3)	1.00
Digit Symbol test	5.43 (±1.8)	5.43 (±1.9)	0.00
Color Trail			
1	3.16 (±0.6)	3.13 (±0.7)	1.00
2	5.96 (±1.2)	6.00 (±1.3)	0.57
Digit vigilance			
Time	3.83 (±1.3)	3.80 (±1.3)	1.00
Error	0.50 (±0.7)	0.57 (±0.77)	1.14
PGI scale	79.00 (±7.2)	79.10 (±7.3)	0.83

Table 6: Neuropsychological functions of both groups (index and control) over three months of follow up.

	Cases Mean (SD)	Follow up Mean (SD)	Controls Mean (SD)	Follow-up Mean (SD)	F
Raven's Matrices	18.86 (±4.8)	19.07(±4.6)	20.13 (±4.7)	20.37 (±4.3)	0.27
Finger Tapping					
Right	29.70 (±3.3)	29.53 (±3.0)	28.80 (±2.7)	28.70 (±2.7)	0.01
Left	29.00 (±3.5)	28.83 (±3.26)	27.60 (±2.3)	27.67 (±2.3)	0.53
Digit Symbol test	7.76 (±2.9)	7.40 (±2.0)	5.43 (±1.8)	5.43 (±1.9)	0.05
Color Trail					
1	4.10 (±1.5)	4.03 (±1.4)	3.16 (±0.6)	3.13 (±0.7)	0
2	7.20 (±2.1)	6.87 (±2.0)	5.96 (±1.2)	6.00 (±1.3)	2.32
Digit Vigilance					
Time	4.33 (±1.1)	4.3 (±1.7)	3.83 (±1.3)	3.80 (±1.3)	0.01
Error	1.16 (±1.5)	0.77 (±1.1)	0.50 (±0.7)	0.57 (±0.77)	1.33
PGI scale	75.43 (±9.6)	75.50 (±9.1)	79.00 (±7.2)	79.10 (±7.3)	0.27

DISCUSSION

In various phases of HIV-AIDS illness, neurocognitive abnormalities have been recorded along several dimensions, with differing severity.[17] According to Grant et al., HIV dementia affects 7-14 percent of participants each year, while psychopathology owing to a lesser type of cognitive impairment, affects half of the individuals with frank AIDS.[18] Though the impairments were moderate in the beginning, they had a cumulative effect on the patient's behavioural adaptation, occupational efficiency, and quality of life.[19] Varied cognitive processes have a different latency in commencement and a different decline pattern. Some of these alterations may have been managed sooner using ARVT.[20]

Previous research has recorded the form and number of cognitive alterations in various stages of the illness, but there have been discrepancies in how ARVT is used to avoid future impairments.[21] As a result, the research was conducted using a Hypothesis-Verification-Design. Both index and control groups were differentiated by their homogeneity and comparability. The determinants of impairment were commonly used neuropsychological instruments with adequate validity that had previously been utilized in the local population.

The current research focused on the most immunosuppressed group (CD-4 count 250-cells) as well as the demographic variables of mostly middle-aged, married males with a high school diploma from both rural and urban areas. Because the majority of individuals who attended the ICTC had a similar socioeconomic profile, these patients may be deemed typical of those who attended. The two groups' comparability was preserved.

When the physical data were compared, it was discovered that the CD4 count and the length of the illness were significantly dissimilar. The difference in CD4 count was predicted since it served as the criterion for separating the index patients from the controls. Longer disease duration in these individuals revealed that rising immunosuppression was a consequence of the illness's length. Biochemical markers such as blood urea and sugar did not differ substantially between the two groups.

When the patients' neuropsychological performance was compared to that of the controls, it was discovered that the patients performed much worse on Color Trail tests 1 and 2 and made significantly more mistakes on the Digit-Vigilance test. The color trail test is a method of determining sustained attention. Digit Vigilance's increased error proneness reveals their failure to maintain focus. Attention disturbances have been established as a characteristic of early neurocognitive abnormalities and fast deterioration in HIV patients.20 Although no significant memory impairment was seen in our experiment, correlations between illness variables and attention loss have been established as contributing to secondary memory issues. Though the impairments were moderate in the beginning, they had a cumulative effect on the individual's

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behavioral adaptation, occupational efficiency, and quality of life.[22]

This study's pattern of neuropsychological abnormalities is comparable to what has been seen in the United States, Australia and Uganda where HIV Clades A, B, and D are widely common.[23] Clade C is the most common in India, and the underlying neuropathology is the same in all clades.

Except for the length of the Digit Vigilance Test and the individual's age, there was no statistically significant correlation between illness variables and neuropsychological performance. Sacktor et al. (2007) [19] found comparable abnormalities in HIV patients as they grew older, concluding that ageing was linked to decreased memory, executive function, and motor performance. They ascribed these discrepancies to alterations brought on by advanced age or by age-related co-morbidities. The HIV-positive participants' CD4 cell count exhibited no significant link with their cognition test results. The findings were similar to those of Salawu et al. (1996),[24] Sunmonu et al.,[25] (2016) and Ayele et al.,[26] (2020). On the other hand CD4 count and attention were discovered to be negatively correlated by Ogunrin et al.,[27] in 2007 and Widyadharma et al. (2017).[28] As per Odiase et al. in 2007,[29] there was a reduction in sustained attention capacity regardless of CD-4 level compared to control patients.

According to an ANCOVA comparing the groups' results in the initial assessment and after three months follow-up, the gains in the index group were not significantly larger than the improvements in the control group in any aspect of neuropsychological functioning. During follow-up, the index group's incremental improvements were insufficient to attain statistical significance. The shortfall may have occurred as a result of the brief follow-up time and may become evident during later assessments.[30] The prospect of improvement may be explained as a consequence of any of the neuropsychological reconstructive processes, and if confirmed in longer follow-up investigations, it might hint at a viable method of avoiding neurocognitive deterioration.

Limitations of the study

- A larger sample number in both groups (index and control) might have improved the generalizability of the findings.
- A more extensive investigation of the pattern of decline and the putative protective impact of ARVT may have been achieved if the groups had been followed up more often over a longer length of time.

CONCLUSION

This research aims to study the prevalence of cognitive impairment among HIV-positive people, examine the pattern of neuropsychological impairment in same patients and investigate the relationship between CD-4 count and cognitive impairment. The index patients had considerably higher impairment in neuropsychological functions compared to controls, according to the study's results. The current investigation found significant impairment in both sustained and focused attention. In terms of mental speed, motor speed, and memory, no significant differences were found. Neuropsychological performance was positively linked with age and duration following positivity. There is no link between CD4 count and cognitive scores. Antiretroviral therapy enhances neuropsychological function, particularly regarding sustained attention and mental flexibility.

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