

# Logistic regression-based parametric analysis of HIV-associated dementia using a screening tool in a tertiary care hospital in Mumbai

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## Abstract

**Context:** The AIDS dementia complex is one of the most common and clinically important complications of HIV infection. Subclinical dementia not presenting with features of frank disease may be missed. The use of screening tools provides a good alternative to a psychiatrist's diagnosis in resource-limited settings like the site of this study. **Aims:** The study aimed to analyze various parameters such as age, gender, duration of the disease, duration since treatment, clinical staging, CD4 count, mode of transmission, and comorbidities like tuberculosis with the prevalence of AIDS dementia complex in the participants. **Settings and Design:** A cross-sectional study involving 180 participants was conducted over a duration of 18 months. **Materials and Methods:** The assessment of dementia was done using the International HIV Dementia Scale. **Statistical Analysis Used:** Backward binomial logistics regression. **Results:** Both duration of treatment and duration since diagnosis of HIV were found to be significantly associated with the presence of AIDS dementia. Patients having stage 4 disease and CD4 counts <200 were likelier to have dementia as compared to other participants. People with an unknown mode of transmission had higher odds of having AIDS dementia than persons having a mode of transmission as via blood/blood products/invasive procedures/mother-to-child transmission/IV drug abuse. Binomial logistic regression revealed mode of transmission or rather its awareness to be the strongest contributor. **Conclusions:** These findings highlight the need for early screening and diagnosis of HIV-associated dementia in patients living with HIV and that of early assessment and initiation of treatment.

**Key words:** Dementia, HIV/AIDS, International HIV Dementia Scale, Mumbai

## Introduction

As per the India HIV Estimation 2019 report, in India, there were an estimated 23.48 lakh (17.98 lakh– 30.98 lakh) people living with HIV (PLHIV) in 2019. Maharashtra was estimated to have the highest number of PLHIV (3.96 lakh).<sup>[1]</sup> The AIDS dementia complex is one of the most common and clinically important complications of HIV infection.

HIV-associated dementia (HAD) is more prevalent in PLHIV who have severe immunosuppression, high viral loads in the cerebrospinal fluid, and advanced HIV as indicated by anemia and hypoalbuminemia.<sup>[2]</sup> PLHIV having HAD are seen to have poorer abilities when it comes to self-care including drug regimen adherence, compared to those without HAD with a lesser median survival time.<sup>[3]</sup>

Early identification of HAD and the treatment of underlying HIV is associated with better neurocognitive outcomes and higher survival rates for PLHIV.<sup>[4]</sup>

Overt dementia is often picked up by the treating physician but underlying subclinical dementia may be missed. The use of screening tools provides a good alternative to a psychiatrist's diagnosis in resource-limited settings like the site of this study. The International HIV Dementia Scale (IHDS) is one of the most widely used screening scales for HAD which has good reliability and validity as tested in various countries around the world.<sup>[5,6]</sup>

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## Materials and Methods

### Duration and participants

A cross-sectional study was conducted over a duration of 18 months at the antiretroviral outpatient department of our institute.

The inclusion criteria involved all HIV-positive patients above 12 years of age, with HIV-1 or HIV-2 positive status. The exclusion criteria included history or examination suggestive of cerebrovascular accident, central nervous system infections like meningitis and encephalitis, Parkinson's disease, or history of previously diagnosed primary psychiatric disorder.

An approval was taken from the institutional ethics committee and National AIDS Control Organization. One hundred and eighty participants were enrolled in the study. Written informed consent or assent was obtained. Consecutively, HIV-positive patients were enrolled in the study irrespective of whether on ART or not.

### Procedure and assessment of dementia

The assessment of dementia was initially undertaken using 2 scales: the Mini Mental Status examination scale (MMSE) and the IHDS. The validity of MMSE in subcortical disease has been criticized and thus its application as a screening tool is discouraged.<sup>[7]</sup> Hence, the MMSE scoring was not used for further analysis and its findings will not be mentioned henceforth.

### International HIV Dementia Scale

IHDS is an interviewer-administered performance measure that assesses 3 domains: motor speed (timed finger tapping), psychomotor speed (timed alternating sequence test), and memory recall (recall of 4 items). Patients with a total score  $\leq 10$  should be evaluated further for possible dementia with the gold standard being a psychiatric evaluation.<sup>[8]</sup>

Patients who had an IHDS score of  $< 10$  were included in the group: patients with possible AIDS dementia and rest of the patients categorized as patients without AIDS dementia.

### Data analysis

Data were analyzed after dividing patients into two groups, i.e., patients with possible AIDS dementia and patients without possible AIDS dementia (based on their IHDS scoring). The variables considered were their age, gender, time since diagnosis, duration of therapy, CD4 count, use of zidovudine, mode of transmission, and presence or absence of tuberculosis as a comorbidity. Continuous data were categorized, and univariate analysis was done for the aforementioned factors using the Chi-square test. Odds ratios were calculated for individual categories. Variables found to be statistically significant with  $P < 0.05$  were considered for backward stepwise binomial logistic regression. All analysis was conducted using SPSS version 28 [IBM Corp (International Business Machines Corporation). Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY (New York): IBM Corp - United States of America].

## Results

Out of a total of 180 participants, 143 were found to be patients without AIDS dementia [Table 1]. 37 patients had AIDS dementia according to the criterion (20.55%).

The mean age of all participants was 43.17 years. Among patients with and without AIDS dementia, the mean age was 43 and 44 years, respectively.

Age ( $\chi^2 = 0.205$ ,  $P = 0.903$ ) and sex ( $\chi^2 = 0.287$ ,  $P = 0.592$ ) were not significantly associated with AIDS dementia at a significance level of 0.05.

Both duration of treatment ( $\chi^2 = 16.789$ ,  $P = 0.002$ ) and duration since diagnosis ( $\chi^2 = 16.072$ ,  $P = 0.001$ ) of HIV were found to be significantly associated with the presence of AIDS dementia at a significance level of 0.05. Patients diagnosed within the past year had statistically significant odds of having AIDS dementia as compared to patients diagnosed between 3 and 6 years ago (odds ratio [OR] = 4.83 [95% confidence interval (CI) = 1.47–15.87]). Patients who were started on treatment within the past year had statistically significant odds of having AIDS dementia (OR = 11.29 [95% CI = 2.30–55.47]) as compared to patients started on treatment 3–6 years ago. The same was found to be true for patients not receiving treatment at all (OR = 9.81 [95% CI = 1.53–40]). However, the patient's current treatment status ( $\chi^2 = 2.726$ ,  $P = 0.099$ ) was not found to be significantly associated with AIDS dementia.

Zidovudine use did not have a statistically significant association with the presence of AIDS dementia ( $\chi^2 = 3.239$ ,  $P = 0.72$ ).

The WHO clinical stage was found to be significantly associated with possible AIDS dementia ( $\chi^2 = 34.109$ ,  $P < 0.001$ ). Patients having stage 4 disease were more likely to have AIDS dementia than patients with stage 1 disease (OR = 13.75 [95% CI = 4.85–39.01]). The presence of tuberculosis as a comorbidity was also found to be significantly associated with AIDS dementia ( $\chi^2 = 13.762$ ,  $P < 0.001$ ; OR = 4.14 [95% CI = 1.89–9.05]).

The possible mode of transmission of HIV was categorized as sexual, others (including blood/blood products/invasive procedures/mother to child transmission/IV drug abuse), and not known with certainty. It was found to have a statistically significant association with the presence of possible AIDS dementia ( $\chi^2 = 6.026$ ,  $P < 0.049$ ). People with an unknown mode of transmission were found to have statistically significant higher odds of having AIDS dementia than persons having a mode of transmission as mentioned under 'others' (OR = 8.64 [95% CI = 1.03–72.55]).

CD4 count was found to be statistically significant in its association with possible AIDS dementia ( $\chi^2 = 22.100$ ,  $P < 0.001$ ). Patients with CD4 counts of  $< 200$  were found to have significantly increased odds of having AIDS dementia as compared to patients with CD4 counts of more than 400 (OR = 15.26 (95% CI = 3.44–67.78)).

Binomial logistic regression was performed with the variables: duration since diagnosis, duration since treatment, CD4 counts, presence or absence of TB, clinical stage, and mode of transmission [Table 2]. The Step 1 model was selected as being most accurate ( $-2 \log$  likelihood ratio = 91.338; Nagelkerke R square = 0.569), which included the variables: duration since diagnosis, duration since treatment, CD4 counts, presence or absence of TB, clinical stage, and mode of transmission. It showed an 87.8% overall accuracy and 66.7% accuracy in predicting possible AIDS dementia [Table 3]. Mode of transmission was found to have the strongest association (largest difference in model with term removed) followed by duration of treatment and clinical stage [Table 4].

**Table 1: Statistically significant associations based on univariate analysis of all parameters (n=180)**

Variable	Possible AIDS dementia		$\chi^2$	P	OR (95% CI)
	Yes	No			
Duration since diagnosis (years)					
Up to 1	20	30	16.072	0.001	4.83 (1.47-15.87)
1-3	4	24			
3-6	4	29			
>6	9	60			
Duration of treatment (years)					
No treatment	9	19	16.789	0.002	9.81 (1.53-40)
Up to 1	13	19			
1-3	4	30			
3-6	2	33			
>6	9	42			
WHO clinical stage					
1	5	82	34.109	<0.001	1
2	0	1			
3	6	29			
4	26	31			
Presence of TB as comorbidity					
Present	26	52	13.762	<0.001	4.14 (1.89-9.05)
Absent	11	91			
Mode of transmission					
Sexual	24	100	6.026	0.049	4.32 (0.55-33.97)
Others	1	18			
Unknown	12	25			
CD4 counts (n=165)					
0-200	26	46	22.100	<0.001	15.26 (3.44-67.78)
201-400	5	32			
>400	2	54			

CI=Confidence interval; WHO=World Health Organization; OR=Odds ratio; NA=Not available; TB=Tuberculosis

**Discussion**

With the widespread use of HAART in developing countries in the mid-1990s, there was a dramatic fall off in the rates of AIDS dementia<sup>[9]</sup> with cases usually associated with specific risk factors including female sex, being elderly, higher HIV viral titers, low CD4+ counts,<sup>[10]</sup> non-use of HAART, lower socioeconomic group, substance abuse, and iron-deficiency anemia.<sup>[11,12]</sup> Along these lines, this was the first study of its kind examining possible HIV dementia purely through a screening tool (IHDS) in an urban tertiary care setup in Mumbai. The prevalence of possible AIDS dementia in our study was found to be 20.55%, which was lower than the prevalence found in other Indian studies like the one conducted by Saini *et al.*, which described a prevalence of 32.50% for HAND.<sup>[13]</sup> This difference could be explained possibly by differences in individual population characteristics and alterations based on the sample size. Age and sex were not found to be significantly associated with AIDS dementia, which also corroborates other studies such as one by Sevigny *et al.*,<sup>[14]</sup> Nakku *et al.*,<sup>[15]</sup> and Habib *et al.*<sup>[16]</sup>

Patients with a longer duration since diagnosis and longer durations of treatment were both found to have statistically significant associations with the presence of AIDS dementia. One explanation for this might be poorer control of disease in recently diagnosed subjects due to poorer health-seeking behavior as compared to their counterparts in this group, resulting in their possible exclusion from routine screening measures in tertiary care setups. The possibility of patients harboring the infection for much longer periods of time than they are aware of should be taken into consideration when interpreting data related to duration of HIV illness. Although

**Table 2: Accuracy of the first step of backward stepwise binomial logistic regression model (n=164)**

Observed Step 1	Predicted		Percentage correct
	Dementia status		
	Absent	Present	
Dementia status			
Absent	122	9	93.1
Present	11	22	66.7
Overall percentage			87.8

<sup>a</sup>The cut value is 0.500

untreated disease is a well-known risk factor for AIDS dementia and it is suggested that early initiation of treatment may also result in superior or preserved neurocognitive performance,<sup>[17]</sup> our study did not find such an association possibly due to a smaller number of subjects having possible AIDS dementia.

Our study examined the use of zidovudine among patients and its association with AIDS dementia and we found no statistically significant association between the same. The effect of CNS penetration of ART drugs as described by their CNS penetration effectiveness rank (CPE), its subsequent impact on AIDS dementia, and the role of CPE in the management of AIDS dementia remains a controversy despite considerable research.<sup>[18-20]</sup> Zidovudine has a CPE rank of 4 (tenofovir = 1, emtricitabine = 3, lamivudine = 2) and hence was selected to study any possible association of CPE rank on AIDS dementia.

Clinical staging also had a significant association with the development of AIDS dementia, concurrent with the

**Table 3: Variables in the binomial logistic regression model (step 1 of backward stepwise regression) (n=164)**

Step 1*	B	SE	Wald	Df	Sig	Exp (B)	95% CI for Exp (B)	
							Lower	Upper
Duration since diagnosis (years)								
Upto 1	-0.009	1.697	0.572	3	0.903			
1-3	-0.757	1.405	0.290	1	0.590	0.991	0.036	27.560
3-6	-19.954	7992.108	0.000	1	0.998	0.000	0.030	7.370
Duration of treatment (years)								
Upto 1	-1.687	1.259	5.808	4	0.214			
1-3	-2.847	1.409	1.795	1	0.180	0.185	0.016	2.184
3-6	-2.731	1.330	4.081	1	0.043	0.058	0.004	0.919
>6	17.344	7992.108	4.215	1	0.040	0.065	0.005	0.883
WHO clinical stage								
Stage 1	-3.346	1.102	9.224	2	0.010			
Stage 2	-0.482	0.678	0.504	1	0.478	0.035	0.004	0.305
TB present								
TB present	-0.845	0.921	0.841	1	0.359	0.430	0.163	2.335
Mode of transmission								
Sexual	-1.419	0.751	3.566	2	0.168			
Others (blood/blood products/MTCT/IV drug abuse/invasive procedures)	-22.704	8644.143	0.000	1	0.998	0.000	0.071	2.612
CD4 count								
0-200	-0.331	0.694	6.834	2	0.033			
201-400	-2.481	0.949	0.228	1	0.633	0.718	0.184	2.800
Constant	4.453	1.754	6.834	1	0.009	0.084	0.013	0.537
			6.442	1	0.011	85.861		

\*Variable (s) entered on step 1: Duration since diagnosis, duration of treatment, clinical stage, TB status, mode of transmission, CD4 count.  $\chi^2$ ue; SE=Standard error; Wald=Wald test; Df=Degrees of freedom; Sig=Significance probability (P); Exp(B)=Exponentiation of the B coefficient; CI=Confidence interval; WHO=World Health Organization; MTCT=Mother to child transmission; IV=Intravenous; TB=Tuberculosis

**Table 4: Impact of removal of individual variables on the model (n=164)**

Variable Step 1	Model log likelihood	Change in-2 log likelihood	df	Significance of the change
Duration since diagnosis	-48.690	6.043	3	0.110
Duration of treatment	-53.008	14.678	4	0.005
WHO clinical stage	-51.602	11.867	2	0.003
TB status	-46.096	0.855	1	0.355
Mode of transmission	-57.936	24.534	2	<0.001
CD4 count	-50.836	10.334	2	0.006

\*Based on conditional parameter estimates. Df=Degrees of freedom; WHO=World Health Organization; TB=Tuberculosis

findings of other studies.<sup>[21,22]</sup> HIV encephalopathy is considered an AIDS defining illness; however, similar considerations have not been made for AIDS dementia.<sup>[23]</sup> We found an increased prevalence in patients with clinical stage 4. However, 29.72% of cases belonged to a lower clinical stage (1-3), which emphasizes the need to incorporate routine screening for AIDS dementia even in the absence of symptoms suggestive of cognitive dysfunction or Stage 4 HIV illness. In lower resource settings where psychiatrist interview is not available routinely, IHDS has been shown to be a reliable tool and can be utilized as part of the routine patient interview.

The relationship between CD4 count and AIDS Dementia is well established,<sup>[10]</sup> and our study also bears witness to this association with the highest prevalence being found in subjects with CD4 counts <100. This also emphasizes the need for thorough CD4 count regulation to prevent the development of AIDS dementia and further morbidity due to it.

The presence of tuberculosis as a comorbidity was found to be statistically significant in its association with AIDS dementia. This may be attributed to tuberculosis itself being

more prevalent among patients with lower CD4 counts and hence advanced disease. A poorer control of disease represented by the presence of tuberculosis may further indicate a more pressing need to assess for AIDS dementia in these subjects.

Patients with an unknown mode of transmission were also found to have a higher incidence of AIDS dementia as compared to those with known modes of transmissions. The patients belonging to the latter groups may undergo more frequent screening and diagnostic testing for HIV as compared to their counterparts with unknown modes of transmission, due to them being construed as “high risk” for the disease, which may result in earlier detection in these patients and subsequent establishment of treatment. This may be further interpreted as a need for more widespread education regarding HIV and its transmission to ensure timely testing.

Mode of transmission was found to be the strongest predictor based on binomial logistic regression. This finding however may be interpreted in the context of disease duration, health-seeking behavior, and knowledge of the illness all affecting a person’s awareness of their mode of transmission and hence resulting in the particularly observed strength of association in this population.

**Limitations**

During the time duration of this study, viral load was being done only for selected patient groups at our center. Hence, the correlation of viral load with AIDS dementia cannot be analyzed in this study.

Socioeconomic data were not analyzed in this study. In scales such as MMSE, the educational status of the patient plays a role in interpreting the outcome. Although the IHDS does not have such a caveat in its interpretation, socioeconomic factors may affect outcomes related to AIDS dementia and were not analyzed in this study.



## Conclusions

The prevalence of possible AIDS dementia complex in our study was 20.55%. The incidence of AIDS dementia declined as the duration from diagnosis of HIV increased. Longer duration of treatment has benefitted HIV-positive patients with respect to the development of AIDS dementia. Patients in the late stages of HIV infection, low CD4 counts, an unknown mode of transmission, and tuberculosis were more likely to develop AIDS dementia. The IHDS is a good screening tool for AIDS dementia in HIV clinics, especially in low-resource settings.

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## Conflicts of interest

There are no conflicts of interest.

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