Original article

Prevalence and factors associated with neuro cognitive disorders among HIV-positive patients in Ethiopia: A hospital-based cross-sectional study

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Abstract

Background: The majority of people living with HIV/AIDS (PLWHA) reside in low- and middle-income countries. HIV-associated neuro-cognitive disorders (HAND) are among the most common neurological complications, especially in resource-limited countries. HAND occurs in all stages of HIV infection, but the risk increases with advanced infection. This study measures the magnitude of HAND and associated factors among HIV patients.

Methods and Materials: A hospital-based cross-sectional study was employed among 581HIV-positive patients using a systematic random sampling technique to select participants. The International HIV Dementia Scale (IHDS) was used to assess cognitive impairment. The collected data were coded and entered into Epi-data 3.1 and analyzed using SPSS version 20.0. Bivariate and multivariate analysis was carried out and interpreted using odds ratio and 95% confidence interval at *p*-value < 0.05.

Results: Five hundred and eighty-one HIV patients were involved in this study, making the response rate 99.49%. Of the total participants, 35.6% had HAND. Being illiterate (AOR: 5.16; 95% CI: 2.20-12.07), having a primary-level education (AOR: 3.27; 95% CI: 1.46-7.29), having a CD4 count (cells/µl) ≤ 500 (AOR: 1.61; 95% CI: 1.11-2.39) and the lifetime use of tobacco (AOR: 2.40; 95% CI: 1.44-4.01) were significantly associated with HAND.

Conclusions: A high prevalence of HAND was observed. Being illiterate, a primary-level education, and a low CD4 count and tobacco use were significantly associated. [*Ethiop. J. Health Dev.* 2020; 34(1):22-29]

Key words: HIV-associated neuro-cognitive disorder, International HIV Dementia Scale, Ethiopia

Introduction

Human immunodeficiency virus (HIV) is the causative agent of acquired immunodeficiency syndrome (AIDS), which is a multi-system disorder involving the central nervous system (CNS) (1). It causes a wide range of neuro-cognitive complications grouped under the acronym 'HAND' (HIV-associated neuro-cognitive disorders) (2). One of the most frequent complications is the disruption of neuro-cognitive function (3), which leads to vulnerability to the cognitive effects of other conditions (4). HIV-associated dementia (HAD) is the most severe manifestation of HIV-associated neuro-cognitive disorder (HAND) (5).

Several studies have estimated the prevalence of HAND to range from 20% to 50%, despite effective antiretroviral therapy (ART). The disorder has an effect on social and work interactions, reduces the patient's adherence to ART, increases the risk of cognitive decline, and ultimately leads to deterioration in quality of life, according to a study conducted in Germany (6). It has long been recognized that the direct effects of HIV on the brain lead to neuro-cognitive impairment and, if left untreated, progress to HAD (7).

More than 70% of the world's HIV-positive population lives in sub-Saharan Africa. HIV-positive individuals throughout this region tend to have worse neuropsychological function (8). HAND may include neurological disorders of various severities. prevalence of HAND in HIV/AIDS patients in Western countries is 10-24% (9).

In a cross-sectional study conducted in Switzerland, there was a prevalence of HAND in 74% of patients with evidence of cognitive decline (10). Poor immunological status, reflected by lower nadir CD4 cell count, has been associated with neuro-cognitive impairment before and after HAART (3). According to study conducted in Brazil, the prevalence of HAND among HIV/AIDS patients was 22.7% (11). Increasing age (OR: 1.104; 95% CI: 1.054-1.155, $p<0.001$), lower educational level (OR: 0.78; 95% CI: 0.69-0.89, $p<0.001$) and lower baseline CD4 count (OR: 0.15; 95% CI: 0.03-0.74, $p<0.001$) were associated with HAND (10, 12). HAND, even in its mild form, is associated with lower medication adherence, a decreased ability to perform the most complex daily tasks, poor quality of life, and difficulty obtaining employment. The prevalence of HAND among HIV/AIDS patients as found to be around 33.3% according to study done in Ethiopia (13).

According to studies done in northern Nigeria and multi-center study conducted by student at Pittsburgh University the prevalence of HAND among HIV/AIDS patients was 21.5% (95% CI = 17.6-25.4) and 34.45%, respectively. In these study cognitive impartment was significantly associated with low CD4 count, high viral load, low level of education, being confined to bed, and poor adherence to ART in the past (9, 14) . According to study done in Yaoundé, Cameroon, it was found that 22.2% of study participants had HAND (15). HAND increases morbidity and health burden and significantly decreased the quality of life (8). Study done in different

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area shows lower level of education and decreased CD4 count was significantly associated with HAND among HIV/AIDS patients (16) (1) (17, 18).

Study done in Malawi, the prevalence of HAND was ranges from 19% to 52% in patients on combination anti-retroviral therapy in high resource settings, and from 14% to 64% in low resource settings (19). In a study of HIV-positive outpatients in Uganda, nearly one third met the criteria for HAD, with advanced age and low CD4 (18). In a South African study, 25% of HIV-positive individuals on combination ART met the criteria for HAD, and an additional 42% met the criteria for mild neuro-cognitive disorder (MND) (20).

In Ethiopia, different studies of HIV-positive patients show that 35.7% in south west Ethiopia (Jimma), 24.8% in north west Ethiopia (Debre Markos), 36.4% in South Wollo and 33.3% in northern Ethiopia (Mekelle) had HAND. Age, level of education, medication adherence and CD4 count were statistically significant (13, 21-23).

Starting highly active anti-retroviral therapy (HAART) early may decrease the progression of HIV and increase CD4 count. But still there is high level of HAND. So, the aim of this study was to determine the prevalence and associated factors of HAND among PLWHIV. Showing the prevalence of HAND and the factors associated with it may prove useful to stakeholders and policy-makers working in neuro-psychiatry.

Methods and Materials

Study design and area: This hospital-based cross-sectional study design was employed among HIV-positive patients visiting the ART clinics of four federal hospitals in Addis Ababa, Ethiopia, from April-May,2018. The four federal hospitals are Amanuel Mental Specialized Hospital, St. Paul's Millennium Medical College, St. Peter TB Specialized Hospital, and Alert Hospital. All hospitals are under the administration of the federal government of Ethiopia.

Sample size and sampling techniques: The respondents were all HIV-positive patients attending the ART clinics of the four federal hospitals during the study period. The sample size was determined using the formula for a single population proportion by taking the prevalence of HAND (36.4%) from a study done in Debre Birhan Hospital, with 95% confidence level and 4% degree of precision. Then, by adding 10% of non-response rate, the final sample size totaled 584. A systematic random sampling technique was employed. The sampling interval was determined by dividing the total study population who had to follow-up during one-month data collection by the total sample size. Proportional allocation of the sample was made at all four hospitals (Figure 1).

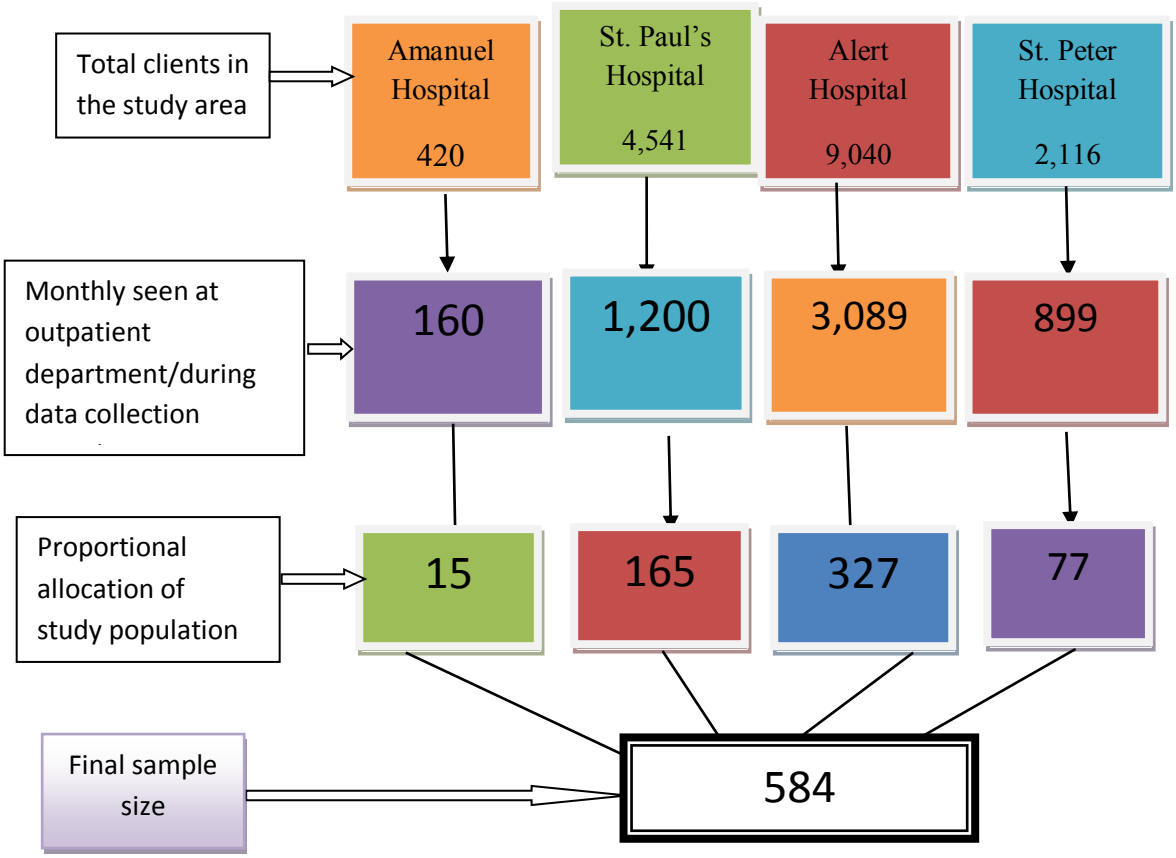

Figure 1: Schematic presentation of proportional allocation of samples of HIV positive patients at four federal hospitals in Addis Ababa, Ethiopia: 2018 (n=581)

Data collection tools and quality controls: Data were collected using a standardized structured questionnaire. The questionnaire was first prepared in English, then translated into Amharic, and finally back-translated into English to maintain the consistency of the questionnaire.

Data quality control issues were ensured by conducting a pre-test on 5% of the study participants. Training was given to data collectors and supervisors on the questionnaire, and on how to screen for HAND using IHDS. They were also informed of the purpose of the study and how to approach respondents and obtain consent. All of the data collectors working in the ART clinics held educational diplomas and had experience of data collection. Filled-in questionnaires were checked daily for their completeness and consistency by the principal investigator and supervisor.

The IHDS consists of three sub tests: timed finger tapping, timed alternating hand sequence test and recall of four items. For words not recalled, the subject had been prompted with a 'semantic' clue as follows: animal (dog, a piece of clothing (hat), vegetable (bean), and color (red). A half-point was assigned for each correct word recalled after prompting. A total score out of 12 was calculated for each participant, with each of the three subtests contributing 4 points to the total score.

HIV associated neuro-cognitive disorder (HAND) was measured by the sum of a 3 item IHDS score. Any patient who score less than or equal to 9 has HANDs. The tool is internal consistent to measure what we want to study with a cronbachs`s alpha of 0.76.

Depression was assessed using the PHQ-9 scale. PHQ-9 is a nine-item self-report instrument. Scoring ranges from 0 to 27, and a score ≥5 indicates having depression. Medication adherence was assessed using an eight-item Morisky Medication Adherence Scale, according to which low adherence is a score <6, medium adherence is a score of 6 or 7, and high adherence is a score of 8. Perceived HIV stigma by the sum of perceived HIV stigma scale of 11-item score greater than or equal to mean, social support by the sum of Oslo 3-item, current substance use who use any substance for the last 3 months, ever substance use who ever uses any substance in their lifetime. Co-morbidities were explained by the presence of confirmed medical conditions or other opportunistic infections (OIs).

Data analysis

The collected data were coded, checked for completeness, edited, cleaned and entered into Epi-data 3.1 and exported to SPSS version 20.0 for analysis. Frequencies, proportions and cross-tabulations were used to summarize descriptive statistics.

All variables which were significant at bivariate analysis were entered into multiple logistic regression to control for confounding factors. Finally, the variables which had a significant association were identified on the basis of AOR, with 95% CI and a *p*-value less than 0.05 to fit the final regression model.

Results

Socio-demographic characteristics: Five hundred and eighty-one respondents were included in the study, making a response rate of 99.49%. Of those, the majority 356 (61.3%) were females and 260 (44.8%) were married. The mean age of the respondents was 37.99 years (±9.83 standard deviation). Of the study participants, 418 (71.9%) were living with families, 261 (44.9%) were Amhara by ethnicity, 362 (62.3%) were Orthodox Christians, 242 (41.7%) had a primary-level education, and 127 (21.9%) were illiterate **(Table 1).**

Table 1: Socio-demographic characteristics of HIV positive patients at ART clinics of the four federal hospitals of Addis Ababa, Ethiopia: 2018(N= 581).

Variables	Categories	Frequency	%
Sex	Male	225	38.7
	Female	356	61.3
Age	18-25	70	12
	26-35	142	24.4
	36-45	143	24.6
	46-55	62	10.7
	≥56	164	28.2
Marital status	Single	169	29.1
	Married	260	44.8
	Divorced	103	17.7
	Other	49	8.4
Level of education	Illiterate	127	21.9
	Primary	242	41.7
	Secondary	143	24.6
	College and above	69	11.9
Religion	Orthodox	362	62.3
	Muslim	124	21.3
	Protestant	81	13.9
	Others	14	2.4
Income	< 500	158	27.2
	501-1,000	150	25.8
	1,001-2,008	128	22.0
	>2,009	145	25.0
Occupation	Governmental	185	31.8
	NGO	135	23.2
	Merchant	101	17.4
	Private	108	18.6
	Jobless	52	9.0
Ethnicity	Amhara	261	44.9
	Oromo	171	29.4
	Tigrayan	66	11.4
	Others	83	14.3
Who do you live with	Alone	137	23.6
	With families	418	71.9
	With social	26	4.5

Prevalence of neuro-cognitive disorders

The prevalence of HAND was 35.6% (95% CI: 31.5-39.8), i.e. those who scored 9.5 or less on IHDS (Figure 2).

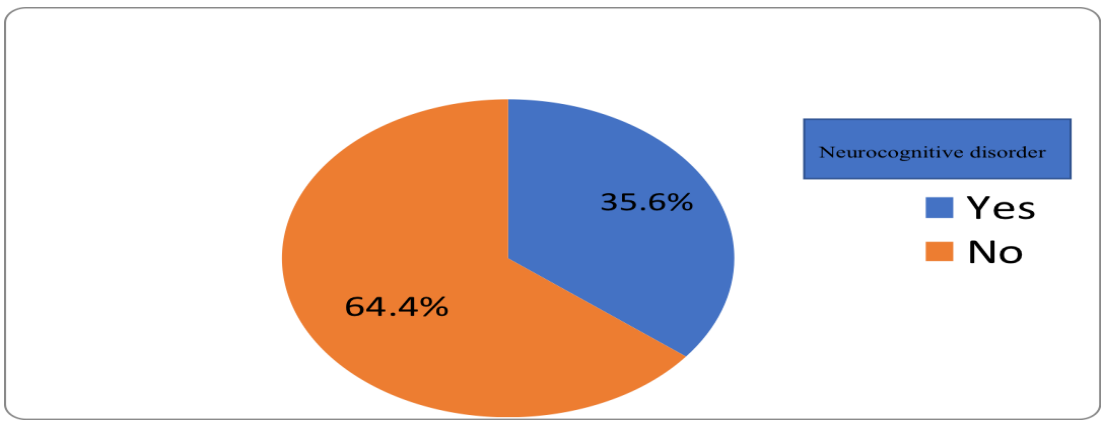

Figure 2: **Prevalence of HAND among HIV-positive patients at four federal hospitals in Addis Ababa, Ethiopia: 2018 (n=581)**

In terms of the IHDS, 103 participants (17.7%) scored 4 out of 4 in the timed finger tapping sub-test to assess motor skills; 132 (22.7%) scored 4 out of 4 to assess psychomotor speed; and 142 (24.4%) scored 4 out of 4 to assess memory recall.

Factors associated with neuro-cognitive disorders: The clinical data reviewed during the time of study shows that 467(80.4%) patients had poor adherence of ART drugs, and 253 (43.5%) had taken less than 5 years duration on ART. In this study, 287 (49.4%) of the respondents had a CD4count of 500cells/µl or less and majority of participants were in stage I HIV 302(52.0%)

Our study shows 355(61.1%) has moderate social support and 308(53.0%) high perceived stigma. In this study, 120 (20.7%) of the respondents had current alcohol use followed by 112(19.3%) lifetime tobacco use (**Table2**).

Table 2: **Distribution of people living with HIV by their factors at four federal hospitals in Addis Ababa, Ethiopia: 2018 (n=581)**

Variables	Categories	Frequency	%
Depression	No depression	437	75.2
	Has depression	144	24.8
Social support	Poor social support	178	30.6
	Moderate social support	355	61.1
	Good social support	47	8.1
Perceived stigma	No stigma	273	47.0
	Has stigma	308	53.0
Current Substance use			
Alcohol use	No	461	79.3
	Yes	120	20.7
Khat use	No	539	92.8
	Yes	42	7.2
Tobacco use	No	524	90.2
	Yes	57	9.8
Others	No	569	97.9
	Yes	12	2.1
Life time substance use			
Tobacco use	No	469	80.7
	Yes	112	19.3
Alcohol use	No	385	66.3
	Yes	196	33.7
Khat use	No	501	86.2
	Yes	80	13.8
Other	No	566	97.4
	Yes	15	2.6
Adherence	Poor adherence	467	80.4
	Good adherence	114	19.6
Duration on ART	<5	253	43.5
	5-10	242	41.7
	>10	86	14.8
	≤ 500	287	49.4
	> 500	294	50.6
HIV stage	Stage 1	302	52.0
	Stage 2	236	40.6
	Stage 3	35	6.0
	Stage 4	8	1.4
Co-morbidity	Yes	115	19.8
	No	466	80.2

Based on bivariate analysis, the socio-demographic variables of sex, educational status and income, and clinical variables such as WHO HIV stage, current tobacco use, lifetime tobacco use, perceived stigma, and CD4 count, were significantly associated with HAND. These variables were fitted into a multivariate binary logistic regression model in order to control for the effect of confounders. In the multivariate regression analysis a p-value <0.05 was considered a significant association.

The results of multivariate binary logistic regression show that being illiterate and having a primary educational status, lifetime tobacco use, and a CD4 count ≤500 cells/µl were factors associated with HAND.

Respondents who were illiterate were 5.2 times more likely to have HAND compared to those with an educational status of diploma and above (AOR=5.16; 95% CI: 2.20-12.07), and those with a primary

education were 3.3 times more likely to have HAND compared to those with a diploma and above (AOR=3.27; 95% CI: 1.46-7.29).

In participants with a CD4 count less than 500 cells/µl, the odds of developing HAND were 1.6 times greater than those with a CD4 count ≥500cells/µl (AOR=1.61; 95% CI: 1.11-2.39) (Table 3).

Table 3: **Bivariate and multivariate logistic regression analysis showing the associations between factors and HAND among HIV-positive clients at four federal hospitals in Addis Ababa, Ethiopia: 2018 (n=581)**

Variables	Categories	HAND		COR (95% CI)	AOR (95% CI)
		Yes	No		
Sex	Male	68	157	1	1
	Female	139	217	1.48 (1.03 - 2.11)	1.22 (0.82 - 1.80)
Educational status	Illiterate	65	62	6.98 (3.19 - 15.28)	**5.16 (2.20 - 12.07)****
	Primary	96	146	4.30 (2.08 - 9.25)	**3.27 (1.46 - 7.29)***
	Secondary	37	106	2.32 (1.05 - 5.15)	1.81 (0.78 - 4.22)
	Diploma and above	9	60	1	1
Income(Birr)	≤500	90	68	4.87 (2.93 - 8.08)	3.28 (0.88 - 5.69)
	501-1,000	45	105	1.58 (0.93 - 2.67)	1.13 (0.64 - 2.01)
	1,001-2,008	41	87	1.73 (1.01 - 2.99)	1.57 (0.87 - 2.80)
	≥ 2,009	31	114	1	1
HIV stage	Stage 1	91	211	1	1
	Stage 2	99	137	1.67 (1.17 - 2.39)	1.19 (0.78 - 1.82)
	Stages 3 and 4	17	26	1.51 (0.78 - 2.93)	1.08 (0.51 - 2.30)
CD4 count (cells/µl)	≤500 cells/µl	116	203	1.51 (1.08 - 2.13)	**1.61 (1.11 - 2.39)***
	>500 cells/µl	91	171	1	1
Perceived stigma	Yes	123	185	1.49 (1.06 - 2.10)	1.22 (0.83 - 1.79)
	No	84	189	1	1
Lifetime tobacco use	Yes	25	87	0.45 (0.28 - 0.73)	**2.40 (1.44 - 4.01)***
	No	182	287	1	1
Current tobacco use	Yes	13	44	0.50 (0.26 - 0.95)	0.79 (0.33 - 1.94)
	No	194	330	1	1

Notes: **p*-value<0.05; ***p*-value=0.000; 1.00 = Reference; Hosmer and Lemeshow goodness-of-fit = 0.73

Discussion

HIV associated neuro-cognitive disorder in HIV/AIDS patients is one of the most common neurological condition especially in resource-limited continents like Africa. It ranges from as low as 10- 24% up to as much as 85%. HAND even in its mild form is associated with decrease medication adherence, and daily activity performance, poor quality of life and unemployment.

The prevalence found in this study was in line with study done in Botswana (38%), Uganda (31%), and Ethiopia (36.4%, 33.3% and 35.7) (24-26).
In most cases, the common factors associated were low level of education, lower CD4 count.
However, the risk of HAND in our study was higher than a study done in North West Ethiopia (24.8%), South Africa (25%), Central Africa Republic (25%), Cameroon (22.2), Northern Nigeria (21.5%), Malawi (15%) and Brazil (22.6%) (9, 14, 15, 26-29). The differences might be accounted to the neuro virulence strain differences.

On the other hand, this study was lower than study done in Switzerland (83%) (10). This difference in the prevalence rate might be accounted to the neuro virulence differences, differences in the method, and cut-off points of measuring instruments.

Our study revealed that being illiterate and primary level of education was 5.16 and 3.27 times higher risk of developing HAND as compared to those who had a diploma and above educational backgrounds [AOR=5.16 95%CI: 2.20 - 12.07], [AOR=3.27 95%CI: 1.46 - 7.29] respectively. This finding was in line with the study done in South Asia, Northern Nigeria, Central African Republic and Ethiopia (9, 14, 26, 30). This could be due to an individual with high level of education level have better awareness health issues and their consequences than those who had low level of education.

Study participants with CD4 count ≤ 500 cell/µl were about 1.6 times more likely affected by HANDs than those cd4 count >500 cell/µl, [AOR=1.61 95%CI:1.11-2.39]. This finding was also in line with study done in Uganda (15), Central African Republic (14), Yaoundé Cameroon (15), Northern Nigeria (9), Ethiopia (26), and Brazil (29). This could be due to the fact that decrease CD4 count can expose to increasing susceptibility to brain infection and neuro cognitive impairments.

Regarding the relationship between life time tobacco use of respondent and HANDs, those who use tobacco in their lifetime has 2.4 times risk for HANDs as compared to those who never use tobacco in their lifetime [AOR: 2.40 95%CI: 1.44-4.01].This could be due to the effect of tobacco on brain cells which kills and stops forming of new brain cells. This finding was in line with study done on USA, and against the study done on Botswana (24, 31).

Conclusion

Our study revealed, high prevalence of HAND in HIV positive patients in Addis Ababa, Ethiopia.

Being illiterate, lower level of education, CD4 count ≤ 500cell/µl, and life time tobacco use were significantly associated with HAND among HIV/AIDS patients. Screening for HAND is crucial, in all clinical service for HIV/AIDS patients giving special attention for these having lower level of education, low cd4 count, and tobacco users**.**

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