HIV dementia among HIV positive people at Debre markos hospital, Northwest Ethiopia

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Abstract: *Background*: HIV dementia which impairs life by causing learning, memory, behavioral and motor disabilities is still a particular problem in the HAART era. It has been prevalent particularly in the third world and specifically in sub Saharan Africa where limited access to diagnosis, treatment, care and support has been common. Hence the assessment of HIV dementia in one of the sub Saharan countries, namely Ethiopia, particularly in Debre markos referral hospital is important. *Methods*: A cross- sectional study design with descriptive and analytical components was employed on 423 participants with systematic random sampling technique (with proportional allocation). Data was collected by face to face interview, observation and document review using International HIV dementia scale translated into local language (Amharic version); then it was analyzed using SPSS window 20. The level of association was dealt using confidence interval and odds ratio. *Result*: the prevalence of HIV dementia was 24.8%. Having no education (AOR=3.11, 95% CI (1.37, 7.04)), older age of 50 years or above (AOR=4.25, 95% CI (1.05, 17.18)), having co morbid opportunistic infection (AOR=7.48, 95% CI (4.1, 13.64)) and substance use (AOR=4.64, 95% CI (2.3, 9.36)) were significantly associated with HIV dementia. *Conclusion*: Despite wide spread use of HAART, HIV dementia among HIV positive people is high when compared to worldwide figure. Having no education, older age of 50 years or more, being on HAART, having co morbid opportunistic infection, being in late stages of the illness and substance use were significantly associated with HIV dementia. *Recommendation*: starting HAART in those who developed opportunistic infection and in those 50 years or older PLHA should be considered regardless of the CD4 count.

Keywords: HIV Dementia, Neuro Cognitive Deficit, Neuro AIDS

1. Introduction

HIV dementia is characterized by memory, learning, behavioral and motor disabilities that interfere with normal daily life and in extreme cases lead to total disability and a bedridden state, and at worst to death. With the advent of highly active antiretroviral therapy (HAART), a less severe dysfunction, minor cognitive motor disorder, has become more common than ADC [1]. Prior to the advent of highly active antiretroviral therapy (HAART), dementia was a common source of morbidity and mortality in HIV-infected patients [2]. It was usually observed in the late stages of acquired immunodeficiency syndrome (AIDS), when $CD4^+$ lymphocyte counts fall below 200 cells/mL, and was seen in up to 50% of patients prior to their deaths. In 1986, the term AIDS dementia complex (ADC) was introduced to describe a unique constellation of neurobehavioral findings [3], [4].

The overall psychosocial and emotional burden on the family and friends of patients with HIV dementia is tremendous, far beyond that of a cognitively intact patient with AIDS. Patients with cognitive difficulties have problems with compliance and adherence to their medication regimen. Because of their neuropsychiatric problems, these patients are likely to be less inhibited and are more prone to HIV-related risk behavior (e.g. unprotected intercourse), and

they therefore pose a greater risk of transmission of the virus [3], [4], [5]. Unlike Alzheimer's- and stroke-induced dementia, HIV associated dementia is treatable and potentially reversible with the same antiretroviral medication that is used to treat the infection [6].

Cognitive impairment could interfere with HIV control; at the very least it can lead to poor adherence, and at worst to disability and death. In fact, poor adherence alone is important, as there is a direct relationship between inadequate levels of antiretroviral drugs and the development of resistance. Failure to recognize cognitive impairment will not only impair individual therapy but will harm the efforts to control HIV in a community, as cognitively impaired patients are less inhibited and are more likely to engage in HIV-related risk behavior. This may be compounded if the transmitted strains are also resistant to HAART [7] [8], [9].

It not only disrupts jobs and ads to the cost of care, but also interferes with a patient's ability to adhere to a regular course of antiretroviral medication, thus increasing the risk of drug resistance. People with dementia also are less likely to practice safe sex [10]. Of the estimated 40 million adults and children worldwide who are living with HIV infection, an estimated 27 million live in sub-Saharan Africa [10], [11], [12], [13].

HIV dementia is the most common cause of cognitive decline in HIV-infected patients. Its prevalence increases with declining immune function, but can be seen as initial AIDS defining illness, with CD4 in range of 200-500cell/ml [14], [15]. Higher risk was found in patients older than 50 years [16], [17]. Depending on sensitivity of criteria used, it has been detected in 25% to 90% of all patients with AIDS; and minor neuro cognitive deficits have been seen at all stages of HIV [18], [19].The prevalence was estimated to be 7.3% in pre-HAART era. Multicenter AIDS Cohort Study Group reported a 7% annual incidence in AIDS patients and a 15% cumulative incidence between AIDS diagnosis and death [16], [18].

Strongest predictors of HIV dementia elicited by Center for disease prevention and control (CDC) are CD4 count less than 100cells/µL, and onset of other AIDS-defining infection/neoplasm. Aggressive treatment of the systemic disease has decreased the incidence (although perhaps not the prevalence) of this HIV complication [18].

In the third world where there are limited resources, and there is little access to antiretroviral therapy (ART), HIV dementia has received scant attention, and it is because of under diagnosis, or it has been considered insignificant [18], [19]. Sub Saharan Africa is the region where highest figure of new infections and the highest number of AIDS related deaths are recorded [20]. In2010, about 68% of all people living with HIV resided in sub-Saharan Africa, a region with only 12% of the global population. Sub-Saharan Africa also accounted for 70% of new HIV infections in 2010, although there was a notable decline in the regional rate of new infections [20], [21].

The first study of HIV dementia on the African continent using international HIV dementia scale (IHDS) done in Uganda reported that 31% of HIV-positives were found to have HIV dementia. The risk of HIV dementia was significantly associated with those people who were older (age > 50 years), and with those patients who had more advanced HIV disease (CD4 cell counts below 200 cells/µL) [16], [17], [18].

According to the cross-sectional study conducted in Yaoundé, Cameroon using the IHDS, the predictors of HIV associated dementia were advanced clinical stage, low CD4 count especially $CD4 \leq 200$ and low hemoglobin concentration [21].

Studies conducted in Malawi and Botswana found that, prevalence of HIV dementia was 14% and 38% respectively; and also male gender and low education level were independent risk factors in Malawian study [28]; whereas increased age and lower educational status were the predictors at Botswana study [29].

Ethiopia has a large and very vulnerable population, with an estimated 15 percent of the population living below the poverty line. HIV/AIDS is one of the key challenges for the overall development of Ethiopia, as it has led to a seven-year decrease in life expectancy and a greatly reduced workforce. HIV prevalence has declined to about 3.2% from 4.7% percent in urban areas [22].

Based on reports taken from VCT centers, blood banks, and ART programs, the cumulative number of people living with HIV/AIDS (PLHA) in Ethiopia is about 1.32 million (45% male and 55% female). This results in a prevalence rate of 3.2% (3% among males and 4% among females; 10.5% urban and 1.9% rural areas) for the total estimated population [23].

The HIV type common in Ethiopia is HIV-1, subtypes C [23].But almost there is scarce data on HIV dementia in the nation.

Generally, HIV dementia is an important complication to diagnose in patients with HIV/AIDS for several reasons:
- it is associated with an increased risk of mortality
- the presence of dementia can affect adherence to HAART, and
- HIV dementia is a potentially treatable condition with highly active antiretroviral therapy

A report on a case control study that assessed neuro cognitive behavior among non treated HIV patients conducted in Ethiopia was found in which inconsistent result was found.

Hence, this study was conducted to assess prevalence of HIV dementia among HIV positives and the factors associated with it.

2. Methods

2.1. Study Design and Period

Institution based cross-sectional study was conducted in Debre-Markos Referral Hospital from April 23 to May 18, 2012 for about a month using quantitative data collection method.

2.2. Study Area

Debre-Markos, the capital of East Gojjam Administrative Zone is located in the north west of the capital city of Ethiopia, Addis Ababa at a distance of 300Kms and 265Kms to the capital of Amhara Nation Regional State, Bahir Dar. As regards the population composition of the town though the Amhara Population is predominant other nations and nationalities also dwell in Debre-Markos. Debre-Markos referral hospital is the only hospital not only in the town but also in east Gojjam zone serving as a referral center for more than a million people. It provides ART service for around 10,000 PLHA who come from different areas, and from this figure those who are currently on HAART (at the end of November) were around 2618, and the rest 7826 PLHA are on pre ART. There are 4 outpatient units that provide ART service in the hospital with average visit 36-40 patients to each unit. The total average visits to ART clinic monthly are 3400 – 3600.

2.3. Study Population

Source population: all PLHA who are following ART service (both pre-ART and On HAART) in east Gojjam, Amhara region, Ethiopia.

Study population: all PLHA that follow ART service (both pre-ART and on HAART) at DMRH ART clinic and who visit ART clinics during the study period

2.4. Variables

2.4.1. Dependent Variable
HIV associated dementia (yes/no)

2.4.2. Independent Variables
-Age   - HIV/AIDS clinical stage,
-Sex   - CD4 count,
-Marital status   - ART status
-Education level   - OIs,
-Occupation   - Treatment regimen
-Religion   - Substance use
-Ethnicity

2.5. Operational Definition

2.5.1. HIV Dementia
Any client with a score of 10 or less on IHDS is screened as having HIV dementia

2.5.2. Substance Use

2.5.3. Ever Use of a Substance
Any psycho-active substance use for non-medical purpose in the last 12 months regardless of the dose and duration

2.6. Inclusion/Exclusion Criteria

Inclusion criteria: age between the ranges 18 to 64 years (since age related dementia starts from age 65 years)

Exclusion criteria: those unable to hear, to communicate or to see,
-acutely disturbed clients, and also
-anyone who has severe disability on his hand (like amputation)

Sampling Method: Systematic random sampling technique was employed. Clients attending ART clinic were allocated in the study proportionally according to their population size as pre ART and on HAART.

Sample size: is calculated using the formula

$$n = z^2pq/w^2$$

With 10% contingency, the final sample size was 423.

Allocation: with proportional allocation, the study participants were 317 and 106 from pre ART and on HAART respectively.

2.7. Data Quality Control

Translation: The questionnaire was translated into local language (Amharic) from its English version then back to English with the guidance of a psychiatrist

Training was provided for the data collectors for one day on how the data should be obtained and recorded.

Pre test: Pre-test was done on 25 HIV positive people at DMRH before the actual data collection time in order to see for the validity of the instrument, to estimate the time needed to collect data, and to modify the questionnaire accordingly. And the treatment regimen was modified by encompassing the newly added first line regimens '1e' and '1f'.

Supervision: Data collectors were supervised while collecting the data by the principal investigator and technical support was provided accordingly.

Data were checked daily for completeness and consistency throughout the data collection period.

Data collection: Data was collected by trained staff Nurses who work in ART clinic by face to face interview, observation and document review from April 23 to May 18, 2012.

Instrument: data was collected using International HIV Dementia Scale (IHDS) which was translated into local language (Amharic version). The IHDS has been a useful screening test to identify individuals at risk for HIV dementia. It consists of three subtests: timed finger tapping, timed alternating hand sequence test, and recall of four items at 2 min. A total score out of 12 was calculated for each participant, and any participant with a score of 10 or less was screened as at risk for dementia, hence, they were recommended to be evaluated further for possible dementia.

Data analysis: Data was coded and entered into epidemiological information (Epi info) then it was exported to statistical package for social sciences (SPSS) 20 program for analysis; descriptive summary using frequencies, proportions, graphs and cross tabs were used to present study results. Odds ratio (OR) and confident interval was used to determine the strength of association between

independent and dependent variables. Those variables with p value 0.2 or less were selected for further analysis. Binary logistic analysis was finally used while to control confounding effect and those variables with P-value less than 0.05 were considered as statistically significant.

Ethical consideration: Ethical clearance was obtained from Institutional Review Board of School of graduate studies, College of Health Science, University of Gondar. Following the endorsement from the university, study setting (DMRH) was informed about the objectives of the study through a support letter from the Institutional Review Board. Each participant was then informed about the purpose of the study and his/her right not to participate in the study was respected. Privacy and confidentiality was assured. After obtaining Informed consent (written) from clients, data was collected. Any participant, who was screened as having HIV dementia, was recommended to be evaluated further for possible dementia back to the clinicians.

3. Results

Socio-demographic characteristics: The respondents were predominantly female 253(59.8%). A quarter of them 107(25.2%) lie in the age group between 25-29 years whereas the mean age and standard deviation of participants was 33.9 ± 7.8 years with a range of 18 to 54 years. Regarding educational status, 130 (30.7%) of them can't read and write. On the other hand 93 (22%) and 91 (21.5%) were daily laborer and government employee by occupation respectively. Married participants were 187 (44.2%). Also 397(93.9%) and 386(91.3%) were Amhara by ethnicity and Orthodox Christian by religion respectively.

HIV Dementia: The prevalence of HIV dementia was 24.8%. The score on international HIV/AIDS dementia scale (IHDS) is as follows.

The first part on IHDS is timed finger tapping, on this part motor speed is assessed, and nearly half of them, 208(49.2%) did well scoring 4 out of 4. But 41(9.7%) and 5(1.2%) did worse scoring 2 and 1 out of 4 respectively. On the next part which assessed psychomotor speed, 181(42.8%) worked well without any impairment scoring 4 out of 4, and 8(1.9%) scored 1 out of 4 respectively.

Memory recall was assessed in the third part, and it was found that 217(51.3%) recalled all the four things without any clue scoring 4 out of 4, but about 73(17.3%) need 2 or more clues to recall all the 4 things.

Clinical factors: about 66 (15.6%) of them were in the late stages of HIV (stage 3 and stage 4). The mean CD4 count was 431 cell/dl with a range of 9 to 1002 cells/dl, and it was also found that 46 (10.9%) of them had CD4 count less than 201cell/dl whereas 146 (34.5%) had more than 500cell/dl.

Also 75 (17.7%) of them had opportunistic infections, and the commonest infections reported were respiratory tract infections which encompass pulmonary tuberculosis, pneumonia, PCP (pnuemocistic carinii pneumonia) and recurrent upper respiratory tract infection which were seen among 36 (8.5%) of the participants. Tuberculosis was the OI reported among 26 (6.1%) of the study participants.

In addition 30 (28.8%) had been on HAART for more than 3 years, but 13 (12.3%) of them for 6 or less months. The treatment regimen for those on HAART shows that 27 (29.4%) and 27 (25.5%) of them were following the first line treatments, 1e and 1c respectively, also 1 (0.9%) participant was on second line treatment.

Substance use assessment: Even though people who are living with HIV/AIDS are not expected to use psycho active substances for non medical purposes, 53 (12.5%) of them had used substance in the last one year. Alcohol was the commonest substance used by 47 (11.1%) of them. Tobacco and Khat use were also reported by 5 (1.2%) and 7(1.7%) of the study participants respectively.

3.1. HIV Dementia and its Associated Factors

A total of 5 variables in the above which had significant association and the insignificant one whose p value was 0.2 or less (marital status (p value = 0.14) were selected for further analysis and entered to binary logistic regression so as to control confounding effect.

The model summary showed that the Hosmer and Lemeshow test was 47.9% showing that the model was fit, and 4 of the 5 variables were significantly associated.

The final result revealed that older age was associated with HIV dementia in which the probability of those 50 years old or above to develop HIV dementia was about 4 times higher than those who were 49 years old or less (AOR = 4.25, 95% CI (1.05, 17.18)). Also the probability of developing HIV dementia among those who can't read and write was about 3 times higher than those who had diploma and above (AOR = 3.1, 95 % CI (1.36, 7.1)). Whereas the probability of developing HIV dementia at primary, secondary, or diploma and above educational level the same.

Having OIs was also associated with HIV dementia in which those who had OIs develop HIV dementia with a probability of about 7 times higher rate than those who had no OIs (AOR=7.48, 95% CI (4.1, 13.64)).

As reported in the above, 53 (12.5%) of the study participants had used substances in the last 1 year, and it was found to have association with development of HIV dementia in which the probability of developing HIV dementia was about 5 times higher for those who used substances than non users (AOR = 4.64, 95% CI (2.3, 9.36)).

On the other hand marital status was not associated with HIV dementia (AOR=1.05, 95% CI (0.62, 1.79)).

Table 1. Adjusted logistic regression analysis among different factors and HIV dementia, DMRH clinic, May 2012

Variable	HIV dementia		Crude OR (95%CI)	AOR (95% CI)
	Yes	No		
Age				
-<50 yrs	99	314	1	1
->=50 yrs	6	4	4.76 (1.32, 17.2)**	4.25 (1.05, 17.18)**
Educational status				
-Can't read & write	47	83	3.54 (1.75, 7.18)**	3.11 (1.37, 7.04) **
-1^0 educ	32	82	2.44 (1.17, 5.08) **	2.1 (0.89, 4.96)
-2^0 educ	14	78	1.12 (0.49, 2.58)	0.99 (0.38, 2.55)
-diploma & above	12	75	1	1
Marital status				
-Not Married	64	172	1.32 (0.84, 2.08)	1.05 (0.62, 1.79)
-married	41	146	1	1
OIs				
-yes	48	27	9.08(5.23, 15.73) **	7.48 (4.1, 13.64) **
-no	57	291	1	1
Sub use				
-yes	30	23	5.13 (2.82, 9.34) **	4.64(2.3, 9.36) **
-no	75	295	1	1

* Significantly associated**;** Hosmer and lemeshow test = 0.479

4. Discussion

Multicenter AIDS Cohort Study Group reported a 7% annual incidence of HIV dementia among AIDS patients and a 15% cumulative incidence between AIDS diagnosis and death. It is between 10-20% in Western countries and has only been seen in 1-2% of India based infections [4], [5], [10].

In this study the prevalence of HIV dementia was 24.8%. A cohort cross sectional study conducted in Uganda among 78 PLHA found that around 31% of the study participants had HIV dementia, and the difference might be accounted to the virus subtypes seen in the regions [4], [5], [10].The common subtypes in Uganda subtype 'D' and 'A', when compared to subtype 'C', the common subtype in Ethiopia, has been associated with risk of developing HIV dementia. Also three-fourth of the study participants was in late stages of the disease in Ugandan study but they were about 15% in this study [5], [10].

The other studies from Malawi and Botswana found the prevalence to be 14% and 38% respectively; the difference might be explained from the difference in study population and demography, in which besides differences in demography those Malawian participants might not be in late stages of the disease, 97.5% of the participants in Botswana were on HAART in which the prevalence of HIV dementia is expected to be high; also the sample size was low [28], [29].

In this study it was also found out that higher age of 50 years or more was significantly associated with development of HIV dementia which is in line with the Uganda and Botswana studies [28], [29]. The possible reason might be accounted to poor response to HAART and also faster progression of the disease at old age.

Similar study conducted in Yaoundé, Cameroon reported that participants in the late stage of the disease and those with CD4 count 200 cell/dl or less were all screened to have HIV dementia [21]. In line to the Cameroon and Ugandan study, it was found that those people who had opportunistic infections were at higher risk of developing HIV dementia than those who had no OIs. As stated in different journals, OIs are developed in late stages of the disease usually when immunity level deteriorates indicating that the person's health status is in danger.

On educational level, inability to read and write (having no formal education) was significantly associated with higher probability of developing HIV dementia than having diploma or above education; and this is in line with the Malawian and Botswana findings [28], [29]. And this might be because relatively better awareness is expected from those who had higher educational level; thus the better the awareness about the illness, the better the early follow up and the better the health status will be.

Those who used any psycho active substance develop HIV dementia at a higher rate than those who didn't use substances. Substance by itself may suppress the immunity level, besides drug interaction and HIV virus; making faster progression of the disease and this might have contributed to the stronger association. This is not yet found by previous studies.

Limitation
- The instrument IHDS was not yet validated in Ethiopia

5. Conclusion and Recommendation

- The prevalence of HIV dementia among PLHA is high at DMRH when compared to the world wide figure
- Having no education, old age of 50 years or more, having OIs , being in late stages of the illness and substance use were significantly associated with HIV dementia

Recommendation

1. To Federal Ministry of health and HIV/AIDS prevention and control office
   - Introducing HAART to those 50 years old or above and in those who had OIs should be considered regardless of the CD4 count
2. To ART clinics and ART clinicians
   - They should adopt HIV dementia screening tools
   - Early diagnosis and aggressive treatment of OIs should be emphasized and special concern should be given to 50 years or older and to those with no education
   - Working hard to stop psycho active substance use through psycho education and other methods should be given a concern
3. To ART service training providers
   - Routine neuro psychological assessments should be incorporated to ART training
4. To the community
   - All people in the community should be educated at least to primary level

Acknowledgment

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