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RESEARCH ARTICLE

PREVALENCE OF EPILEPSY AMONG HUMAN IMMUNO-DEFICIENCY VIRUS (HIV) INFECTED ADULT PATIENTS TAKING ANTIRETROVIRAL THERAPY (ART) IN ADAMA HOSPITAL MEDICAL COLLEGE, OROMIA REGIONAL STATE, ETHIOPIA

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ABSTRACT

Introduction: Epilepsy is one of the recognized Central nervous System (CNS) complications in HIV infected patients. However, so far there were unknown researches conducted regarding the prevalence of epilepsy among HIV infected adult patients in Ethiopia in general and in the study area in particular.

Objectives: The study was conducted to determine the prevalence of epilepsy among HIV infected adult patients who were on Anti-retroviral treatment (ART) in Adama Hospital Medical College, 2017.

Methodology: Hospital based cross-sectional study was conducted using quantitative data collection method. A total of 748 HIV infected adult patients on Anti-retroviral treatment were recruited. Face to face interview was conducted using pretested structured questionnaire to collect the data. The imaging and laboratory results were extracted from Anti-retroviral treatment Logbook using checklist. The collected data was entered using Epi Info version 7 and exported to SPSS version 21 for analysis.

Results: The prevalence of Epilepsy among HIV infected adults patients on ART was 15.4% (95% CI: 12.7, 17.9). The most common opportunistic infections were Cryptococcal meningitis and Toxoplasmosis.

Conclusion and Recommendations: The prevalence of Epilepsy among HIV infected adult patients taking ART is high. The health care providers should take in to account for the need of testing for HIV in adults while diagnosing Epilepsy.

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INTRODUCTION

Epilepsy and Seizures are important neurological complications among Human Immuno-deficiency virus (HIV) infected patients (Browne and Holmes, 2001). Epilepsy is a condition in which someone has unprovoked seizures at two or more separate times in their life (Pascual-Sedano *et al*., 1999). A seizure is an abnormal electrical discharge within the brain resulting in involuntary change in movement, sensation, perception, behavior, and/or loss of level of consciousness (Browne and Holmes, 2001). In most studies, the majority of patients suffered primarily from generalized seizures with only 25% to 30% showing focal symptoms (Pascual-Sedano *et al*., 1999; Wong *et al*., 1990). Focal seizures were not necessarily associated with focal space occupying lesions (Wong *et al*., 1990). Both simple and complex partial seizures are seen in patients with diffuse brain disease, such as HIV encephalopathy and meningitis (Wong *et al*., 1990). In different studies, the incidence of convulsive status epilepticus has been reported between 8% and 18% and often associated with poor prognosis (Wong *et al*., 1990; Holtzman*et al*., 1989; Van Paesschen *et al*., 1995). Human Immuno-deficiency virus infection carries a higher risk of seizure disorders due to central nervous system (CNS) and opportunistic infections (Bhigjee, 2005; Attili *et al*., 2006). The direct harmful effects of HIV on the CNS (Bhigjee, 2005), complications due to medications used for HIV therapy (Pascual-Sedano *et al*., 1999; Attili*et al*., 2006; Chadha *et al*., 2000) and metabolic abnormalities may all predispose HIV patients to seizure development (Wong *et al*., 1990; Bhigjee, 2005). Seizure occurs among 2% to 20% of HIV infected individuals and an increased incidence of HIV infection may be an important cause for seizures (Dal Pan*et al*., 1997). Indeed, the insidence of seizure is 3% in Spain (Pascual-Sedano *et al*., 1999), 5% in India (Chadha *et al*., 2000), 11% in the USA (Wong *et al*., 1990), 3% to 17% in South Africa (Bhigjee, 2005). Study in France has shown 33% of patients infected by HIV presented with epilepsy as neurological manifestation (Bartolomei *et al*., 1999). According to a study conducted in India, the new-onset of seizures were noted in

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20% of the cohort of 500 HIV-sero-positive individuals (Sinha *et al*., 2005). However, the data about prevalence of seizure among HIV infected patients are limited and most studies have small sample size affecting the precision of the estimate.On the other hand, Toxoplasmosis is the most common opportunistic infection of intracranial lesions in AIDS and it occurs in 3-10% of patients in the USA, up to 50% of patients in Europe and 8% in Africa. Also, Cryptococcal meningitis is the most frequent meningoencephalitis producing seizures (Wong *et al*., 1990; Holtzman *et al*., 1989; Van Paesschen *et al*., 1995; Dore *et al*., 1996; Labar and Harden, 1997). Primary CNS lymphoma is also a common cause of AIDS-related intracranial mass lesions, it occurs in up to 2% of patients with AIDS (Report of the Quality Standards Subcommittee of the American Academy of Neurology, 1998). In patients without mass lesions, meningo-encephalitis caused by some opportunistic infections is a frequent cause of seizure (Dore*et al*., 1996; Labar and Harden, 1997). In a case-control study, 84% of patients had prior AIDS-defining illness, and mean CD4 T-cell count was 8 x 106 cells/µl, while in a control group (patients without seizures) mean CD4 T-cell count was 14 x 106 cells/µl, and AIDS-defining illness was present in 80% of the patients (Dore *et al*., 1996). However, as to the best knowledge of the researchers little is known about the situation in Ethiopia in general and study area in particular. Therefore, this study was aimed to determine the Prevalence of epilepsy and possible opportunistic infections among HIV infected adult patients on ART in Adama Hospital Medical College.

METHODS AND MATERIALS

Study area

The study was conducted in Adama Hospital Medical College which is located 100 km from Addis Ababa (the capital of Ethiopia) to the east. HIV infected adult patient care and ART service in Adama Hospital was started almost 14 years ago and a total of 18,167 adult patients are currently on ART and Pre-ART services. Accordingly, 12,650 adult patients were ever started ART and 5,517 are on Pre-ART registration.

Study design and period

Hospital based cross-sectional study was conducted using quantitative data collection method from February 1-March 30, 2017.

Source population

- All HIV infected adult patients who were on ART in AHMC, were the source population.

Study population

- All HIV infected adult patients taking ART in AHMC from February 1-March 30, 2017 were the study population.

Exclusion criteria

- All HIV infected adult patients who developed epilepsy due to genetic and other congenital disorders were excluded from the study.

Sample size determination

The required sample size was determined using single population proportion formula with the assumption of prevalence of Epilepsy (P) among HIV infected adult patients taking ART of 20% taken from study conducted in India (19), confidence level of 95% and precision of 3%. Considering the 10% non-response rate and design effect of two, the following formula was used to calculate the optimumsample size:

$$n = \frac{(Z\alpha/2)^2 * P(1-P)}{d^2}$$

$$n = \frac{(1.96)^2 * 0.2(1-0.2)}{(0.03)^2} = \mathbf{683}$$

Where;

- n = required sample size to determine the prevalence of Epilepsy among HIV infected adult patients taking ART
- p = proportion of Epilepsy among HIV infected adults taking ART,
- d = estimated margin of error for the study
- $Z_{\alpha/2}$ = the corresponding value of confidence coefficient at alpha level of 0.05 that is 1.96

For the possible none response, additional 10% were considered**.** Therefore, the total sample size required for the study was 752.

Sampling procedure

Before sampling, sampling frame was developed using patients Medical Registration Number (MRN) recorded in ART logbook. Samples were selected using systematic random sampling procedure. The interval was determined bydividing the total number of patients tothe sample size, which was found to be 10 (every ten patients were selected) from HIV infected adult patients on ART registration.

Operational definitions

Epilepsy: is a condition in which someone has unprovoked repeated seizures at two or more separate times.

Seizure: is an abnormal electrical discharge within the brain resulting in involuntary abnormal body sensations, movements, perceptions and/or loss of consciousness.

HIV related epilepsy: is when patients had experienced at least two episodes of seizure after HIV infection.

Epilepsy among HIV infected adult patients taking ART: when patient developed epilepsy while taking ART.

Data collection

An interviewer administered structured questionnaire was used for data collection. A questionnaire was prepared in English and translated into *Oromiffa* (the regional working language) and back translated to English by different experts to ensure its consistency. The *Oromiffa* version was pre-tested on 5% of the sample size in similar private Hospital found in the town before the start of the actual data collection. Based on the findings of the pre-test, necessary corrections were made. Data were collected by the three trained nurses having previous data collection experiences. After interviewing the respondents other necessary information like opportunistic infections,

Epilepsy, their laboratory and imaging results were extracted from the ART logbook using checklist.

Data quality assurance

To ensure the quality of data, three days training was given for data collectors. Before starting to collect data, pre-test and translation of questionnaire was done. Frequent follow-up was done by the principal investigator. And necessary corrections were made on the spot. Questionnaires were also checked for completeness and consistencyon daily bases.

Data processing and analysis

Data was coded and entered into Epi Info version7 and then exported to SPSS version 21 for analysis. Data organization presentation and summarization were done as appropriate to answer the objectives. The assumptions for normality of continuous variables were checked to be satisfied.

Ethical considerations

This study was approved by Adama Hospital Medical College Ethical Review Board. A written letter was submitted to ART unit in the College to obtain permission. After explaining the objective of the study verbal consents were obtained from the study participants. Patients were assured for anonymity of the study. By participating in this research, they were assured for not to feel that it has some discomfort especially on wasting their time. They have the right to refuse, ask any question that is not clear and to discontinue at any time.

RESULTS

Socio-demographic characteristics

A total of 748 HIV/AIDS patients on ART unit in Adama Hospital Medical College were included into the study, with the response rate of 99.5%. More than half, 384 (51.3%) of the participants were females. The mean (± SD) age of the respondents was 34.4 (± 10.28) years. Most of the respondents, 253 (33.8%) were in the age group of 29 to 37 years. The majority, 456 (61.0%) of participants were urban dwellers. About two in five, 296 (39.6) were Muslim and about one third, 506 (67.6%) were married and, 505 (67.5%) were Oromo by Ethnicity. Morethan one quarter, 206 (27.5%) of the respondents were self-employed and 272(36.4%) attended College or University (Table 1).

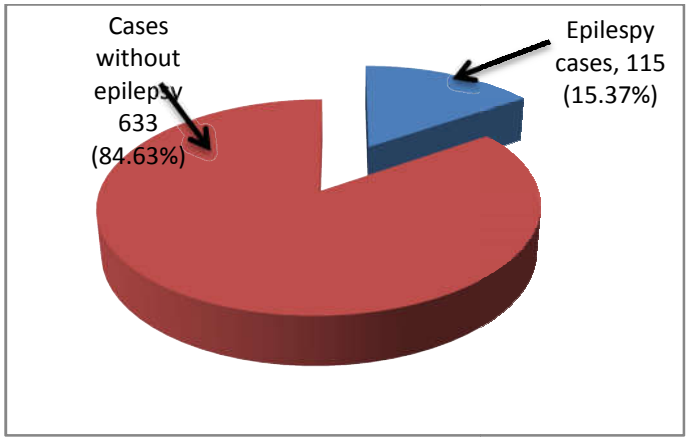

Figure 1. Prevalence of Epilepsy among HIV infected adult patient who were on ART in Adama Hospital Medical College Oromia Regional state, Eastern Ethiopia, 2017

Table 1. Socio-demographic characteristics of participants among adult patient on ART in Adama Hospital Medical College, Eastern Oromia Regional state, Ethiopia, 2017

Variable (n=748)	Frequency	Percent
Age of respondents		
18-26	169	22.5
27-35	263	35.1
36-45	198	26.4
46-55	82	11.0
>56	36	5.0
Sex		
Male	364	48.7
Female	384	51.3
Residence		
Urban	456	61.0
Rural	292	39.0
Religion		
Orthodox	251	33.6
Muslim	296	39.6
Protestant	190	25.4
Others*	11	1.4
Marital status		
Single	197	26.3
Married	506	67.6
Divorced	40	5.3
Widowed	5	0.7
Ethnicity		
Oromo	505	67.5
Amahara	182	24.3
Gurage	51	6.8
Others**	10	1.3
Occupation		
Government employee	202	27.0
Farmer	121	16.2
Self-employed	206	27.5
Student	125	16.7
Others***	163	12.4
Educational level		
Illiterate	35	4.7
Primary	178	23.8
Secondary	263	35.2
Diploma and above	272	36.4

NB: Others include *Catholic and Wakefata, **Tigre, Kambata, ***Homemaker, Retired, NGO employee and Unemployed

Prevalence of Epilepsy among HIV infected patients on ART

Out of 748 HIV infected adults patients taking ART, 115 had been diagnosed to have Epilepsy making the prevalence of 15.4% (95% CI: 12.7, 17.9) (Figure 1).

Types of Epilepsy among HIV infected patients on ART

Further description on the type of Epilepsy showed that, of 115 participants who had Epilepsy, 47 (6.3%) were having focal seizure, 43 (5.7%) had generalized tonic clonic seizure (GCTS), 15 (2%) had tonic-clonic seizure, 8 (1.1%) were having absence Epilepsy and 0.3% were diagnosed to have unclassified seizure.

Opportunistic infections among HIV patients on ART diagnosed for Epilepsy

The major identified opportunistic infections among the respondents were Cerebral Toxoplasmosis and Cryptococcal Meningitis for which each accounted for 27.8%. The other identified opportunistic infections were Tuberculosis Meningitis (14.2%), Ischemic stroke (5.3%), Brain abscess (5.4%), haemorrhagic stroke 5 (4.3%) and head injury (7.8%) (Figure 2).

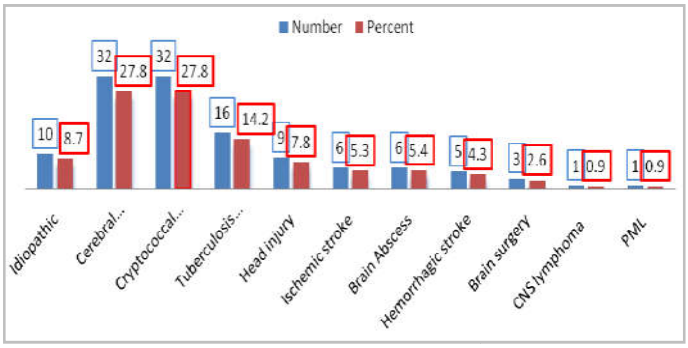

Figure 2. Associated opportunistic infections among HIV infected adult patient who were on ART diagnosed for Epilepsy in Adama Hospital Medical College, Oromia Regional state, Ethiopia, 2017.

Imaging and Laboratory Tests

The CT scan was performed for 108 patients and 97 (89.8%) of them had an abnormal imaging. Moreover, the results of Electroencephalogram (EEG) for 111 patients indicated that for 65 (85.6%) of them had epileptic abnormalities. Also, Brain MRI was performed for 56 patients of which 41(91.1%) had abnormal findings. The results of CD4 count among 748 patients showed, 133 (17.8%) were having CD4 count <200 mm^3 (Table 2).

Table 2. Imaging and laboratory results among HIV infected adult patient who were on ART in Adama Hospital Medical College, Oromia Regional state, Eastern Ethiopia, 2017

Imaging/Investigation	Number	Percept
CT Scan (n=108)		
Normal	11	10.2
Abnormal	97	89.8
EEG findings (n=111)		
Normal	16	14.4
Abnormal	95	85.6
Brain MRI (n=56)		
Normal	5	8.9
Abnormal	41	91.1
CD4 Count (n=748)		
<200 mm3	133	17.8
>200 mm3	242	82.2

DISCUSSION

This study assessed the prevalence of Epilepsy and opportunistic infections among adults infected with HIV/AIDS and put on ART in Adama Hospital Medical College, Oromia Regional State, and EasternEthiopia. The prevalence of epilepsy among adult patients infected with HIV taking ART was 15.4%. This finding is higher compared to a study conducted in Germany showed 6.1% (Holtzman *et al*., 1989), in Korea of 3% (Labar and Harden, 1997), in Cameroon (Yaoundé Central Hospital) of 9.5% (Report of the Quality Standards Subcommittee of the American Academy of Neurology, 1998), in South-West Nigeria of 6.5% (Kellinghaus *et al*., 2008) and in Sudan, Khartoum of 5.71% (Garg, 1999). These differences might be due to differences in socio-demographic status, the timing of the study, immune status and the procedures used to diagnose Epilepsy/seizure. Moreover, the differences might be attributed to whether the patient diagnosed and treated early for HIV/AIDS before their higher CD_4 count becomes lower and severely exposed to different opportunistic infections. Moreover, the findings of this study is higher as compared to a study conducted in south India in which 9.8% of HIV infected drug naïve patients with neurological disorders have new onset of seizures (Wong*et al*., 1990). This difference might be attributed to the fact that in Indian study the patients have not yet started to take ART. In the current study, out of 115 participants presented with Epilepsy, 47 (6.3%) had focal seizure, 43 (5.7%) had generalized tonic clonic seizure (GCTS), 15 (2%) had tonic-clonic seizure, 8 (1.1%) had absence seizure and 0.3% had unclassified seizure. These supports study conducted in Sudan, Khartoum (Garg, 1999) in which among 700 AIDS patients 40, 20, 12, 8, and 20 had convulsion, partial epilepsy, complex partial epilepsy, and generalized epilepsy, respectively. Similarly, in Cameroun, Yaoundé 36 (66%) of patients had generalized seizures, and 34% partial seizures (Wong *et al*., 1990). In India (Pesola and Westfal, 1998) it was shown that 65.2% of patients with generalized seizures and focal seizures accounts for 34.8%. In France it was reported for 71% of generalized seizures and 29% of partial seizures (Rosenbaum *et al*., 1989). In our study, the major opportunistic infections identified among the study participants with Epilepsy among HIV infected adult patients taking ART were Cerebral Toxoplasmosis and Cryptococcal Meningitis corroborating findings from South India, mainly from cryptococcosis and toxoplasmosis affecting the central nervous system (Wong *et al*., 1990). Moreover, it was reported in other study, 30.7% had HIV encephalopathy and 19.2% of toxoplasmosis (Labar and Harden, 1998). But in a study conducted in Khartoum, Sudan, the causes of epilepsy were CNS lymphoma, brain abscess, meningitis, toxoplasmosis encephalitis and PML (Garg, 1999). As to the strengths ofthis research, different diagnostic procedures and tools (CT scan, MRI, EEG and laboratory investigations) were used to identify the possible causes of epilepsy among study participants. Moreover, a reasonable sample size was used to increase the precision of the estimate. As to the limitations of the study, due to thecross sectional nature of the study design there might be impossible to ascertain the possible causation. Moreover, recall bias might also be inevitable.

Conclusion

The prevalence of Epilepsy among HIV infected adult patients taking ART is high (15.4%) as compared to other studies. The major identified opportunistic infections were Cerebral Toxoplasmosis (27.8%) and Cryptococcal Meningitis (27.8%).

Recommendations

Based on the findings, the health care providers should take in to account for the need of testing for HIV in adults while diagnosing Epilepsy. Further study is recommended to justify or nullify the present findings.

Competing interests

The present authors declare that they have no competing of interests.

Authors' contributions

Both authors were responsible for the design and conduct of the study. The statistical analysis, the interpretation of findings and drafting of the manuscript were done by the two authors. The authors read and approved the final content of the manuscript.

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