Prevalence, correlates and under-diagnosis of clinical depression among adults on highly active antiretroviral therapy in a Tertiary Health Institution in northeastern Nigeria

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Abstract

Clinical depression is a highly debilitating illness, which is often under-diagnosed and negatively impacts on the quality of life of its sufferers. When it co-exists with other medical conditions, its effect is even more incapacitating. Undiagnosed depression in the context of HIV infection leads to accelerated decline in CD4+ cell counts with concomitant increase in the viral load and poor adherence to the antiretroviral medications which lead to viral mutation and the evolution of resistant strains. This study examined the prevalence of depression, its correlates and the frequency of the diagnosis of the condition among HIV+ subjects on highly active antiretroviral therapy (HAART) by the internists and general physicians at the University of Maiduguri Teaching Hospital in Northeastern Nigeria.

Three hundred and fifty representative samples of HIV+ adults on HAART were drawn from the Antiretroviral Therapy Clinic of the Institution. Diagnosis of depression was made using the International Classification of Diseases-10 criteria based on Composite International Diagnostic Interview generated data. Socio-demographic and clinical variables were also analyzed for their correlation with depression in the subjects.

About 20% of the respondents were diagnosed with clinical depression and no diagnosis of the condition was hitherto entertained in all the respondents. The independent determinants of depression in the participants were: female gender [odds ratio (OR)=3.87 (95% confidence interval, CI: 2.089-7.183)], past history of psychiatric illness [OR=43.81 (95% CI: 9.731-197.30)] and family history of psychiatric illness in first-degree relatives of the subjects [OR=14.364 (95% CI=5.327-38.729)]. Depression is a relatively common psychiatric condition among adults on HAART, there is therefore the need for routine screening of this condition among HIV+ subjects in order to optimize patient care and improve clinical outcomes.

Introduction

Clinical depression is an incapacitating illness with variable prevalence rates in the general population ranging between 2.1% to 17.4% depending on the country in which the study was conducted and the system of diagnostic classification adopted.[1-3] It is one of the major causes of disabilities because it leads to impairments in the physical, cognitive, and social and/or role functioning domains of livelihood.[4] Thus, depression is not only a hindrance to the sufferer but also a global public health problem. The World Health Organization (WHO) in the year 2000, reported that depression was the fourth highest determinant of the global burden of diseases, it accounted for 4.5% of the *disability adjusted life years*. It was also the second leading cause of disability as it contributed about 12.1% of the *years lived with disability* in Europe, and North America. It has been projected that depressive disorders will be the leading cause of disabilities in the low-income regions of the world by the year 2020.[5]

In the context of HIV/AIDS, highly variable rates of clinical and sub-syndromic depression have been documented among HIV+ subjects since the genesis of the pandemic ranging from 19.4% to 54.3%.[6-10] Despite the variability, meta-analysis has revealed that comorbid depression is almost twice common in people living with HIV (PLHIV) than the general population.[11] The reason for such high figures among PLHIV is that such individuals are subjected to many stressors such as; ambivalence and uncertainty associated with living with a potential fatal disorder, stigmatization and loss of significant members of one's social support network which make psychosocial adjustment difficult.[12,13] Although, the introduction of the highly active antiretroviral therapy (HAART) regimens has significantly increased the life expectancy of persons living with HIV/AIDS, such people are still vulnerable to developing mental illnesses (including clinical depression) because of the persistence of some of the psychosocial stressors earlier mentioned.[14] Some of the significant correlates of depression in PLHIV include; history of depression in the patient as well as family history of depression, acute symptomatic illness, substance abuse, younger age group, female gender, perceptions of HIV-related stigma, and social iso-

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lation.[15,16]

Despite the fact that depression is a relatively common comorbid condition in HIV/AIDS, its detection rate in general clinical settings is still very low. Olisah *et al.* has shown poor recognition of depression in the setting of HIV/AIDS in Nigeria.[8] Similarly, in a study conducted in the United States by Steven *et al*., of a total over 420 patients who had Composite International Diagnostic Interview (CIDI) diagnosis of major depression in the general hospital setting, about 45% of them did not have a documented diagnosis.[17] The findings cited above are pointers to the fact that comorbid depression is grossly under-diagnosed in the setting of most chronic disorders. The negative effects of undiagnosed and untreated depression in HIV infection is associated with accelerated declines in CD4+ cell counts and significant increases in viral load[18,19] and it can lead to poor treatment adherence.[20,21] Poor adherence is directly associated with poor medical outcomes and can also result in the development of viral mutations, which can lead to drug resistance.[22,23]

The aims of this study were to: i) determine the prevalence of clinical depression among HIV+ adults on HAART; ii) determine the socio-demographic and clinical correlates of depression among the subjects; and iii) examine the frequency of the diagnosis of comorbid depression in HIV+ subjects by the general physicians and the internists.

Materials and Methods

This was a cross-sectional study conducted at the outpatient antiretroviral (ART) clinic of the University of Maiduguri Teaching Hospital (UMTH) in Northeastern Nigeria, between May and November 2010. At the time of data collection, the ART clinic had 5574 registered subjects with 3594 of them already placed on treatment with the HAART regime. The sample size was calculated using a prevalence of depression of 35% among HIV+ subjects in northern Nigeria obtained by Shehu *et al*.[24] and was set at 95% confidence interval and 0.05 degree of freedom. The computation yielded a representative sample of 350 subjects. Therefore, the 350 subjects enrolled into the study were selected using the systematic random sampling technique (n^{th} sampling) and a sampling ratio of 1:10 was adopted. Hence, the sampling interval was every other tenth patient until the total number of 350 patients was reached. The list of all patients in the clinic constituted the sampling frame and the starting point on the list was chosen at random using the random number tables. Since the maximum appointment time in the ART is three months, the folders of those subjects who were already interviewed were marked X in order to avoid double recruitment.

The inclusion criteria were: i) adults who were on HAART and who have given their consent to participate; and ii) those on HAART who must be between the ages of 18 and 65 years. The exclusion criteria were: i) those below 18 years of age; ii) those with marked cognitive impairment; iii) those with comorbid chronic or severe physical illnesses capable of impairing their response; and iv) non-consenting adults.

For the purpose of detecting subjects with cognitive impairments, all of them were screened by a single investigator by carrying out a simple cognitive functioning assessment in order to exclude those with cognitive impairment. Thus, the patients were assessed for orientation in time, place and person, attention and concentration, as well as the immediate, recent and remote memories. Based on the outcome of this clinical test alone, those respondents found to have impairments on any of these cognitive domains were excluded.

Ethical consideration

Ethical clearance was obtained from the ethical review board of the University of Maiduguri Teaching Hospital. Written informed consents were also obtained from all the selected subjects. They were informed that their participation was voluntary; they reserved the right to withdraw from the study at any stage and were also assured that their non-participation will not compromise the quality of care they were receiving. In order to ensure confidentiality, codes were used for data entry and analysis.

Measurements

The authors adapted the confirmatory diagnosis of HIV+ results using the STAT-PAK test outcome (ver. 2008; Chembio Diagnostic System Inc., Medford, NY, USA), which is routinely done for all HIV+ subjects as part of the hospital's policy.

An anonymous socio-demographic questionnaire designed by the authors soliciting for the age, gender, occupational status of the respondents using the social class stratification by Borofka and Olatawura was used.[25] This system classified individuals based on their occupations into: social class I (consisting of highly skilled professionals like Doctors, Lawyers, etc.), social class II (consisting of intermediate skilled professionals like, Technicians, nurses, etc.), social class III (consisting of low skilled respondents like junior clerks, drivers, junior military, etc.), social class IV (consisting of unskilled respondents like petty traders, messengers, etc.) and social class V (consisting of unemployed respondents). Other critical information such as marital status, years of education, family history and past history of psychiatric illness were also incorporated into the questionnaire.

The diagnosis of depression was made using the depressive disorder module of the CIDI-World Mental Health Version 3.0.[26] The diagnosis of depression was then made by the authors using the International Classification of Diseases (ICD)-10 criteria by matching the symptoms generated by the CIDI with the ICD-10 diagnostic criteria. This instrument was previously used in Nigeria during the world mental health survey in 2004 and three of the investigators in this study were trained as project supervisors by the Ibadan center of the African regional office of the WHO and are proficient in its use. Permission to use the instrument was also granted by the center. Previous independent studies conducted that compared the degree of concordance between the depressive module of the CIDI and the clinician's diagnosis of depression using either the ICD-10 or the DSM-IV criteria have consistently shown acceptable degree of concordance with Kappa values (K) in the range of 0.71 to 0.93 across different samples, thus making it a valid module for the detection of depression in both clinical and non-clinical samples.[26,27]

Basic clinical information such as; the duration of the illness, the CD4 counts and the CDC staging of the disease were obtained from the respondents' medical records. Information regarding the diagnosis of depression, treatment with antidepressants and any form of psychological intervention were also obtained from their medical records. Depression under-diagnosis in this study was defined as absence of documented diagnosis of depression, and/or treatment with antidepressants or other forms of psychological intervention in the subjects' medical records.

All the instruments were administered to the participants by two of the investigators (who each had at least 5 years training in psychiatry) and were trained in the use of the instruments and were certified to be proficient. An estimation of their inter-rater reliability was calculated initially. Here the two investigators administered the CIDI to 20 patients who did not form part of the main study. Their concurrence on the scores of the various items of the instrument (*i.e.* inter-rater reliability) was calculated using the Hall's method of 1974[28] and a value of 92% was obtained and was considered acceptable.

Statistical analyses

The data were analyzed using SPSS version 16.0. The prevalence of depression was determined using descriptive statistics. Diagnosis of depression was based on the CIDI-generated ICD-10 diagnostic criteria. To assess the predictors of depression in the participants,

bivariate analysis was conducted on all socio-demographic and clinical variables and stepwise logistic regression was subsequently performed on variables that were found to be statistically significant in order to determine the independent correlates of depression. Significance was computed at P≤0.05, two tailed.

Results

Of the 350 subjects who were recruited for the study, the data of only 303 respondents (86.6%) were analyzed. The data of the 47 patients that were not analyzed included those who declined to give informed consent (n=17), those with comorbid debilitating physical illnesses and severe cognitive impairment that affected their response (n=11) and those whose questionnaires could not be analyzed due to missing data (n=19).

Prevalence of depression and the socio-demographic profile of the subjects

Of the 303 HIV+ subjects, 60 (19.8%) of the respondents met the CIDI - ICD-10 diagnostic criteria for depression. One hundred and sixty four (54.1%) were males while, 139 (45.9%) were females. The ages of the subjects ranged from 18 to 54 years with a mean age of 35 years (standard deviation±8.20). Majority of the subjects, 91.4% were less than 40 years of age. Seventy-six (25.1%) of the subjects had formal education while, 123 (40.6%) of them were married. One hundred and ninety-five (64.36%) of the HIV+ subjects on HAART belonged to social classes IV and V. These findings are presented in Table 1.

Socio-demographic and clinical correlates of depression among the subjects on highly active antiretroviral therapy

After subjecting all the variables to bivariate and logistic regression analyses, only female gender, past history of psychiatric illness and family history of psychiatric illness were found to be independent predictors of depression in the study participants. The odds ratio for depression among the female subjects was almost 4 [odds ratio (OR)=3.87 (95% confidence interval, CI: 2.089-7.183)]. The odds ratio for depression among those with past history of psychiatric illness was about 44 [OR=43.81 (95% CI: 9.731-197.30)]. The last independent predictor of depression found among the subjects in this study was family history of psychiatric illness in the first degree relatives of the subjects with an odds ratio of over 14 [OR=14.364 (95% CI=5.327-38.729)]. These findings are presented in Tables 2-4.

Under-diagnosis of depression in HIV+ patients on highly active antiretroviral therapy

Of all the subjects with CIDI-diagnosis of depression, none of them had a documented diagnosis of depression in their clinical records, neither was there any prescription of antidepressants nor referral for any psychological intervention. Thus, the detection rate for depression among the HIV+ subjects was zero percent.

Discussion

The prevalence of depression found among the respondents on HAART was 19.8%, which translates to about every one out of five subjects included in the study had clinical depression. This finding is similar to the prevalence rate of 21% reported by Morrison et al in the USA.[6] It is however relatively lower than the rates of 28.7% and 38.7% reported by Adewuya *et al.* and Olley *et al.*, in southwestern Nigeria and South Africa respectively.[7,9] This lower prevalence may be due to the assertion by Rabkin *et al*.[29] that the availability of HAART causes significant reduction in psychological distress which may predispose to the development of depression. The subjects enrolled for this study have also spent sometimes living with the condition; the average duration on treatment was 27.43±6.5 months. In this case, the respondents have developed some adaptive coping strategies, which might be protective against the development of depression, while the previous studies included patients who were newly diagnosed, yet to commence therapy and come to terms with the reality of their diagnosis. Other landmark studies that determined the prevalence of depression among HIV seropositive subjects with lower rates were that of Alciati *et al.* and Rabkin *et al.* with prevalence rates of 4.4% in Italy and 5-8% in the UK respectively.[14,29] The marked difference in this finding with the outcomes of the other studies may be attributed to differences in cultural and community perception of the disease between Africa and the western societies.

When compared with the prevalence of depression of 3.3% in the general adult population in Nigeria,[2] the rate reported among the subjects on HAART in this study is significantly higher. The possible reasons for the difference may include; the change in status of HIV infection to a chronic disorder and the associated distresses of living with a chronic condition, significant life events such as losses in the form of death of spouses, children, and even loss of support from friends and relatives as a result of stigma, some of the antiretroviral medications may have neuropsychiatric side effects.[30] In addition, the physical complications of the disease may also be contributory as well as the possibility of over diagnosis due

Table 1. Socio-demographic profile of the retroviral positive group (N=303).

Socio-demographic variable	Frequency (%)
Gender	
Male	164 (54.1)
Female	139 (45.9)
Age (mean age=35 years+8.2)	
<20	59 (19.5)
20-29	128 (42.2)
30-39	90 (29.7)
≥40	26 (8.6)
Education	
No education	72 (23.76)
Primary	24 (7.92)
Secondary	46 (15.18)
Tertiary	101 (33.33)
Islamic	60 (19.80)
Occupational status	
Skilled (Social class I)	26 (8.6)
Intermediate (Social class II)	41 (13.5)
Semi-skilled (Social class III)	41 (13.5)
Unskilled (Social class IV)	107 (35.3)
Unemployed (Social class V)	88 (29.0)
Marital status	
Single	63 (20.8)
Married	123 (40.6)
Widow	93 (30.7)
Separated	4 (1.3)
Divorced	20 (6.6)

Table 2. Socio-demographic correlates of depression among patients on antiretroviral therapy (N=303).

Variable	Depressed Frequency (%)	Non-depressed Frequency (%)	Total Frequency (%)	χ^2	P-value
Age group					
<20	14 (23.3)	45 (18.5)	59 (19.5)	7.17	0.067
20-29	28 (46.7)	100 (41.2)	128 (42.2)		
30-39	10 (16.7)	80 (32.9)	90 (29.7)		
≥40	8 (13.3)	18 (7.4)	26 (8.6)		
Gender					
Female	43 (71.7)	96 (39.5)	139 (45.9)	20.04	<0.001*
Male	17 (28.3)	147 (60.5)	164 (54.1)		
Marital status					
Single	11 (18.3)	52 (21.4)	63 (20.8)	4.27	0.371
Married	25 (41.7)	98 (40.3)	123 (40.6)		
Widow	17 (28.3)	76 (31.3)	3 (30.7)		
Separated	0 (0.00)	4 (1.6)	4 (1.3)		
Divorced	7 (11.7)	13(5.4)	20 (6.6)		
Education					
No education	12 (20.0)	64 (26.3)	76 (25.1)	11.14	0.011*
Primary	19 (31.7)	38 (15.6)	57 (18.8)		
Secondary	12 (20.0)	57 (23.5)	69 (22.8)		
Tertiary	17 (28.3)	84 (34.6)	101 (33.3)		
Occupation					
Social Class I	5 (8.3)	21 (8.6)	26 (8.6)	4.32	0.364
Social Class II	5 (8.3)	36 (14.8)	41 (13.5)		
Social Class III	5 (8.3)	36 (14.8)	41 (13.5)		
Social Class IV	25 (41.7)	82 (33.8)	107 (35.3)		
Social Class V	20 (33.4)	68 (28.0)	88 (29.1)		

*Statistically significant findings.

Table 3. Clinical correlates of depression in HIV/AIDS (N=303).

Variable	Depressed Frequency (%)	Non-depressed Frequency (%)	Total Frequency (%)	χ^2	P-value
Duration of illness					
1-3	51 (85.0)	161 (66.3)	212 (70)	8.898	0.012*
4-6	9 (15.0)	70 (28.8)	79 (26.1)		
7-8	0 (0.00)	12 (4.9)	12 (3.9)		
CDC Clinical staging at the time of the study					
Stage I	0 (0.00)	2 (0.80)	2 (0.7)	5.502	0.139
Stage II	1 (1.7)	18 (7.4)	19 (6.3)		
Stage III	30 (50.0)	137 (56.4)	167 (55.1)		
Stage IV	29 (48.3)	86 (35.4)	115 (37.9)		
CD4 count at the time of study					
<200	15 (25.0)	71 (29.2)	86 (28.4)	15.22	<0.001*
200-399	44 (73.3)	122 (50.2)	166 (54.8)		
>400		1 (1.7)	50 (20.6)	51 (16.8)	
Past history of psychiatric illness					
Present	16 (26.7)	2 (0.8)	18 (5.9)	57.52	<0.001*
Absent	44 (73.3)	241 (99.2)	285 (94.1)		
Family history of psychiatric illness					
Present	16 (26.7)	6 (2.5)	22 (7.3)	41.84	<0.001*
Absent	44 (73.3)	237 (97.5)	281 (92.7)		

*Statistically significant findings.

Table 4. Logistic regression analysis for variables significantly associated with depression in HIV/AIDS.

Variable	Odds ratio	95% CI	SE	P-value
Gender	3.873	(2.089-7.183)	0.383	0.002*
History of psychiatric illness	43.818	(9.731-197.30)	0.840	<0.001*
Family history of psychiatric illness	14.364	(5.327-38.729)	0.629	0.002*
CD4 count	0.340	(0.164-0.704)	0.314	0.870
Duration of illness	0.581	(0.248-1.362)	0.422	0.097
Level of education	-	-	0.151	0.514

CI, confidence interval; SE, standard error. *Statistically significant findings.

to the similarities between the somatic symptoms of depression and the physical symptoms of HIV.[31]

The characteristics of the respondents also revealed a preponderance of males to females (54.1% *versus* 45.9%); this is not in keeping with the overall gender distribution of the disease in sub-Saharan Africa, Nigeria inclusive. Results of previous surveys have consistently shown higher rates of HIV positivity in females due to social, economic, cultural and biological factors that increased their vulnerability to infection with the virus. The gender discrepancy found in this study could be due to the economic advantage of males over females thus making more men to come forward for treatment and possible cultural constraints that limit the free movement of women particularly in northern Nigeria without the consents of their husbands or male guardians thus serving as an impediment in terms of their access to health care. Another finding worth commenting on in this study is the fact that over two thirds of the HIV+ subjects belonged to the lower social classes (*i.e.* social classes IV and V). This could be attributed to the free ART and other services offered by the clinic to patients who come forward to access them, thus attracting more people who are less economically empowered. HIV+ subjects who belonged to the higher social classes are likely to seek for treatment in private hospitals or in highly confidential settings in order to avoid the *perceived publicity* associated with their seropositive status and the attendant stigmatization.

Of all the socio-demographic and clinical characteristics of the subjects examined in this study for relationship with the development of depression in PLHIVs, only female gender, past history of psychiatric illness and family history of psychiatric illness have been found to be independent predictors. Similar findings have been reported in previous studies with some degree of consistency as correlates of depression in HIV+ subjects. Females were about 4 times more likely to develop depression in the setting of HIV infection than their male counterparts. This finding is almost similar to that of Gureje *et al.*[2] in which a female to male ratio of 3:1 for vulnerability to depression was reported. Several factors could be attributed to this, but the most conspicuous are; the additional psychosocial stresses faced by women living with a socially stigmatizing illness both at home and at work and the possible role of hormonal factors associated with menstrual cycles, pregnancy and menopause could. In terms of the past history of psychiatric illness, out of the 18 subjects with a history of psychiatric ailment, sixteen developed clinical depression thus making them about 44 times more vulnerable than the subjects without similar history. This is because HIV diagnosis and its attendant inter-current complications and presentations can be potent triggers for depression especially in those with prior history as reported by Buchanan et al who made similar observation.[32] The last independent predictor of depression in the HIV+ subjects identified in the study was family history of psychiatric illness. This finding is consistent with family studies, which have shown that the history of depression in the first-degree relations of a subject naturally increases the subject's vulnerability to developing it. To further support this point, genetic studies have also revealed that the risk of developing depression is increased in the first-degree relatives of both bipolar and unipolar probands, with the risk being about twice greater in relatives of patients with unipolar depression.[33] The genetic predisposition to the development of depression in HIV+ subjects might probably be exaggerated as observed in this study.

Finally, in terms of the under-diagnosis of depression in the HIV+ subjects, the zero percent detection rate obtained in this study was indicative of the fact that neither the internists nor the general physicians routinely assess their HIV+ subjects for this important comorbidity. Secondly, the absence of functional consultation-liaison psychiatric services in the institution that would have encouraged cross-fertilization of clinical ideas between the managing physicians and the mental health experts would have contributed to the under-diagnosis.

Limitations of the study

There is the need for caution in the interpretation of the results of this study as the effects of other significant psychosocial stressors such as stigmatization and other temporally related life events like recent death of spouses and other loved ones due to HIV infection were not separately assessed. Secondly, the HIV+ population in the clinic may not be truly representative of the general HIV+ population in the locality as the clinic offers free antiretroviral drugs and it would have most likely attracted people of the lower socioeconomic classes. Thirdly, the effects of certain antiretroviral drugs on mood were not independently assessed.

Conclusions

Depression is a relatively common comorbid condition among HIV+ patients on HAART and the rate of its detection is low among generalists and the internists. We hereby recommend that a holistic care of people living with HIV/AIDS should include routine assessment of possible comorbid psychiatric conditions, most especially depression, so as to optimize patient care and improve treatment outcome. Furthermore, the setting up of functional consultation-liaison psychiatric units in institutions where such arrangements are non-existent and to strengthen them where they are weak are recommended in order to encourage multi-disciplinary and collaborative approach in the management of patients who may develop concurrent mental ailments in the context of physical disorders.

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