

Adherence to Highly Active Antiretroviral Therapy, in Depressed Peoples Living with HIV/AIDS in Nigeria, West Africa

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Abstract

Objectives: Non-adherence to antiretroviral therapy has serious consequences for prognosis and may lead to the development of resistant strains of the virus. This study determined the prevalence and effect of depressive disorders on Anti-Retroviral Therapy (ART) as well as factors responsible for non adherence in North Central Nigeria.

Methods: This was a hospital based, cross sectional, descriptive study of three hundred adult HIV/AIDS patients attending the HIV clinic of Kwara State specialist hospital, Sobi, Ilorin from 1st April to 30th June, 2013. Respondents were evaluated for various socio-demographic and clinical related variables. The PHQ-9 was administered to screen for depression. Those who scored one and more were assessed clinically for depression. The CAGE questionnaire was used to assess alcohol misuse. A modified version of the Internalized Stigma of Mental Illness scale (ISMI) was used as a measure of self-stigma. Adherence was assessed using self-reporting method. Structured questionnaire was used to evaluate factors responsible for treatment adherence.

Results: One hundred and seventy (56.7%) satisfied the criteria for a depressive disorder using the PHQ-9 score. The adherence rate to antiretroviral therapy was 81%. This represented those who ingested 95% or more of their drugs in the one week preceding the interview. Adherence was higher among non-alcoholics than current or ex-alcoholics. Forgetfulness, 37.1% and stigmatization, 18.2% were the major reasons proffered for non compliance with ART. Stigma had profound effect on the adherence.

Conclusion: Depressive disorder in PLWHA is associated with poor adherence to antiretroviral medication. Early identification and treatment of depression in such patients may improve antiretroviral medication adherence and treatment outcomes.

Keywords: Active antiretroviral therapy; HIV; Depressed people; Nigeria

Introduction

Medication adherence may be defined as the extent to which a patient takes a medication in the way intended by a health care provider [1] and it is expressed quantitatively as the percentage of doses that have been taken by the patients [2]. Adherence to antiretroviral therapy (ART) is of critical importance because even minor deviations from the prescribed regimen can result in viral resistance [3,4]. Studies of ART continue to indicate that a near-perfect adherence is required to adequately repress viral replication [5,6].

Earlier studies of antiretroviral adherence used a minimum level of adherence that was derived from the literature on the level of adherence (>80%) [7], necessary to achieve successful tuberculosis prophylaxis [8]. Many studies subsequently have shown that an even higher level of adherence ($\geq 95\%$) is necessary for durable suppression of HIV-1 virus load [9]. In HAART therapy, adherence of less than 95% has been linked with treatment failure [10]. Lower adherence rates foster development of virus mutations and the risk of developing resistance have been found to be highest with adherence in the range of 80 to 90%. Adherence can be evaluated in several ways [11]. These include pharmacological measures (determination of serum and urinary concentrations of drugs or using biological markers integrated into the tablets), blood test for viral loads; clinical measures (clinical judgment

of the doctor and the use of questionnaires); and physical measures (verifying prescription renewals, counting the remaining pills or pill counting systems). Although, there is no gold standard allowing precise measurement of compliance [12], the electronic pill counter or Medication Event Monitoring System (MEMS) may be considered as the best existing system for measurement of compliance [13]. Pharmacological methods also have a higher sensitivity and specificity [14] but remain difficult to use in practice.

Poor adherence is especially common when a patient has poor knowledge, understanding, and perception of the disease or when a complex drug regime is prescribed [15]. A recent review of compliance

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to antiretroviral drugs reported figures ranging from 28% to 82% with most studies showing rates between 50 and 80% [16].

Different levels of adherence have been reported in earlier studies in Nigeria. For instance, the levels reported for studies conducted in Kano (northern Nigeria), Sagamu, Niger Delta and Benin City (Southern Nigeria) are 49.2% [17], greater than 85% [18], 80% [19] and 58% [20], respectively. In several countries in sub-Saharan Africa and North America, varying levels have also been reported.

Multiple factors influence adherence among patients with HIV/AIDS. Such factors include patients' age, regimen complexity, drug side-effects, advanced HIV disease and patients mental health [21]. Other factors include unfamiliarity with the implications of having a chronic potentially deadly disease, the complex impact of ART on interpersonal relationships, depression and hopelessness, lack of accurate information, and issues related to local cultural frameworks (e.g. illness ideology) [22]. A Ugandan study showed that factors such as lack of transportation and money, stigma, clinical response to therapy, drug packaging and cost may impact on adherence [23]. Long-term viral suppression requires consistent and high percentage adherence accompanied by optimal inter-dose intervals. Efforts to improve viral outcomes should address not only missed doses but wide variations in doses timing [24].

HIV infection can lead to neuropsychiatric syndromes [25]. Clinicians need to be aware of this possibility when evaluating new patients and observing changes in patients whom they treat [26]. Depression is the most commonly observed psychiatric disorder among patients with HIV infection [27]. The prevalence rate of depression in HIV-positive clinic populations ranges from 22 to 32% which is about 3 to 5 times higher than that in the general population [28,29]. Importantly, this may be an underestimation as there is evidence that depression may be under-diagnosed in the context of HIV medical care [30]. HIV increases the risk of developing depressive symptoms through a variety of mechanisms such as: direct injury to subcortical areas of the brain; chronic stress; stigmatization; worsening social isolation; bereavement; debilitation; and intense demoralization [31].

Research suggests that co-morbid depression in patients with HIV/AIDS may be associated with reduced adherence to ART [32], and furthermore with disease progression [33]. A study in Ethiopia found that patients who were not depressed were two times more likely to be adherent than those who were depressed, although the principal reasons given for skipping doses were simply forgetting, feeling ill, being busy and running out of medication. These authors concluded that adherence is a dynamic process which changes over time and cannot reliably be predicted by a few patients' characteristics that are assumed to vary with time [34]. A further study in Tanzania showed that self-reported adherence was high in HIV-positive patients on ART despite economic hardship, depression, low rates of HIV disclosure and high perceived HIV-associated stigma [35]. The authors cited the following factors as key to improving adherence to ART substantial improvement in health condition after starting ART; perceived need to meet family responsibilities; development of specific strategies to remember to take pills; material/emotional support received from others; and regular advice/instruction from health care providers emphasizing adherence.

The rationale for this study was based on the observation by physicians caring for Patients Living with HIV/AIDS (PLWHA) that a significant proportion of patients in treatment have poor adherence to ART despite adequate exposure to medication adherence counseling. It

is highly relevant therefore to investigate possible factors contributing to non-adherence. The aim of this study was to determine the prevalence of depressive disorder in patients with HIV/AIDS and to study its effect on adherence to antiretroviral medication.

Methods

This study was conducted at a designated HIV/AIDS treatment centre in the Kwara State Specialist Hospital, Sobi, Ilorin, Kwara State, located in the North Central Nigeria. The HIV/AIDS treatment centre took off in the hospital in May, 2009. Eight hundred patients have been enrolled and over six hundred are on Highly Active Antiretroviral Therapy (HAART). The centre is currently being founded by an international Non-Governmental Organization (NGO), Friends for Global Health.

This study was a descriptive, cross-sectional study carried out from 1st of April to 30th June, 2013. The inclusion criteria were all HIV positive patients, who presented at the Clinic. The exclusion criteria were the critically ill patients. The sample size was estimated using the Fisher formula [36], using 21.3% from a previous study [37], as the best estimate of depressive disorders among People Living with HIV/AIDS. A minimum size of 218 was calculated using Fisher's formula but 300 was used to increase the power and reliability of the study. Pilot study was carried out at the Kwara State Civil Service Hospital, using 30 respondents (10% of the sample size). Ethical approval was obtained from the Ethical Review Committee of the Kwara State Ministry of Health before commencement of the study. An interviewer administered questionnaire was used. However, for subjects who do not understand English, a local dialect version of the instrument was used. These were arrived at, through the process of translation and back translation by panel of bilingual experts. All patients who agreed to participate in the study were interviewed using the PHQ-9 questionnaire (Appendix A) [38], after thoroughly explaining the procedure to them. Clinical and socio-demographic data were assessed. Four clinical interview questions, the CAGE questionnaire [39] (Appendix B) was used to make a diagnosis of alcoholism. The questions focused on Cutting down, Annoyance by criticism, Guilty feeling, and Eye-openers. Self-reporting methods was used to detect HAART adherence. Adherence was defined as taking 95% of prescribed doses over the previous month which corresponded to missing no more than one does in a 10-day period (in a 2 times a day dosing regimen), one dose per week (in a 3 times a day regimen) or one dose per day (in a once daily does regimen) in a 20-day period. Patients were classified as non-adherent if they missed more than 5% of their doses in at least one of the three categories or if they indicated missed doses in all three categories.

Internalized Stigma of Mental Illness (ISMI) [40] was the questionnaire used in the present study which included 55 items pertaining to internalized stigma, which were abridged to produce the 29-item ISMI. Each statement is assessed on the following 4-point Likert scale: 1=strongly disagree, 2=disagree, 3=agree, 4=strongly agree. Items were grouped theoretically a priori into five subscales: Alienation, Stereotype Endorsement, Perceived Discrimination, Social Withdrawal, and Stigma Resistance.

Completed questionnaire and measurements were entered into a computer data base. The data were analyzed using the epidemiological information (Epi-info) 2005 software package of Center for Disease Control and Prevention (CDC). The 2 by 2 contingency tables were used to carry out Chi-square test and to find out the level of significance and values less than 0.05 were regarded as statistically significant.

Results

Table 1 shows the socio-demographic characteristics of the respondents. A total of one hundred and seventy sero-positive respondents with depression were recruited into the study. The age range 36-40 years had the highest number of respondents 50 (29.4%). Females 139 (81.8%), outnumbered males 31 (18.2%) giving a male: female ratio of 1:4.5. Predominantly, 139 (81.8%) were Muslims, while Christian constituted 30 (17.6%). Fourteen (8.2%), were married while the same number were single. One hundred and sixteen (68.3%) were separated/divorce while 26 (15.3), were widow/widower. The majority of them 56 (32.9%), had no formal education, 55 (32.4%), had primary education while 42 (24.7%) had secondary education. Only 17 (10.0%) attended tertiary institution. Majority, 91 (53.5%), were traders, while 14 (8.2%), were unemployed. Six (3.5%) were students.

Table 2 displays the treatment variables. Sixty eight (40%) were on AZT+3TC+NVP while 5 (2.9%) were on AZT+3TC+LPV/r.

AZT = Zidovudine, 3TC= Lamivudine, NVP= Neviripine, EFV= Efavirenz, TDF= Abacavir.

Table 3 shows that Cotrimoxazole (Septrin) was the commonest used drug for opportunistic infection while 4 (2.4%) were on Fluconazole.

Table 4 shows the common side effect of antiretroviral and opportunistic infection medications. The most common side effect was rashes 27.6%, itching 18.8%, and headache 16.5%. Anaemia was the least experienced side effects.

Figure 1 shows that 130 (43.3%) of the respondents were not depressed, 170 (56.7%) satisfied the criteria for a depressive disorder using the PH-9. Among the respondents, 109 (36.3%) had minimal depression, while 4 (13%) were severely depressed.

Figure 2 shows the clinical staging of the patients. Majoring, 92 (54.1%) were in stage I, 41 (24.1%) in stage II, 26 (15.2%) in stage II and 11 (6.5%) in stage IV.

Table 5 shows the cost implication of treatment to respondents in order to access Anti Retroviral Drugs (ARV). Sixty two (36.5%) had difficulty in paying for clinic expenses while sixteen 16 (9.4%) had difficulty in paying for registration at the clinic, 98 (57.6%) indicated that they lost income by coming to the clinic for appointments. Fifty eight (34.1%) incurred other cost as a result of taking ART.

Figure 3, displays the CAGE questionnaire. Fifty two (30.6%) respondents had at one time or the other engaged in alcohol intake. Twenty seven (52%), respondents scored 4, 13 (25%), scored 3, 7 (13.5%), scored 7, 4 (7.6%) scored 1, while 1 (1.9%) scored 0. In all, 47 (90%) respondents had a total score of 2 or greater which is of clinical significant (sensitivity of 93% and a specificity of 76% for the identification of problem drinking).

Table 6 shows in order of frequency, the reasons proffered by patients for non-compliance with anti-retroviral therapy. The commonest reason include forgetfulness, stigmatization and been away from home.

Table 7 shows that patients' self-report adherence was 81.2%.

Table 8 shows that 103 (60.6%) had minimal stigma while 15 (8.8%) were severely stigmatized.

Variable	N = 170	(%)	
Age group (years)			Mean age is 39y with SD of ± 10.8
< 26	19	11.2	
26 – 30	27	15.9	
31 – 35	20	11.8	
36 – 40	50	29.4	
41 – 45	11	6.5	
46 – 50	19	11.1	
51 – 55	6	3.5	
56 – 60	11	6.5	
>60	7	4.1	
Gender			
Male	31	18.2	
Female	139	81.8	
Ethnicity			
Hausa	39	22.9	
Yoruba	92	54.1	
Igbo	28	16.5	
Others	11	6.5	
Religion			
Christianity	30	17.6	
Islam	139	81.8	
Traditional	1	0.6	
Marital Status			
Single	14	8.2	
Married	14	8.2	
Separated/Divorced	116	68.3	
Widowed/Widower	26	15.3	
Educational level			
Non-Formal	56	32.9	
Primary	55	32.4	
Secondary	42	24.7	
Tertiary	17	10.0	
Occupation			
Trader	91	53.5	
Civil servant	16	9.4	
Self employed	43	25.4	
Unemployed	14	8.2	
Students	6	3.5	
Monthly Income (N)			
No Income	20	11.8	
≤20000 (\$125)	129	75.9	
20001-30000 (\$187)	10	5.8	
30001-40000(\$250)	6	3.5	
40001-50000(\$312)	3	1.8	
>50000 (\$312)	2	1.2	

Table 1: Socio-Demographic Characteristics of Respondents.

Combinations	Frequency	Percentage (%)
AZT+3TC+NVP	68	40
AZT+3TC+EFV	34	20
4DT+3TC+NVP	13	7.6
TDF+FTC+EFV	28	16.5
TDF+FTC+NVP	15	8.8
ABC+3TC+NVP	7	4.2
AZT+3TC+LPV/r	5	2.9
Total	170	100

Table 2: Treatment Variables of HIV Patients at the Specialist Hospital, SOBI, Ilorin, Nigeria.

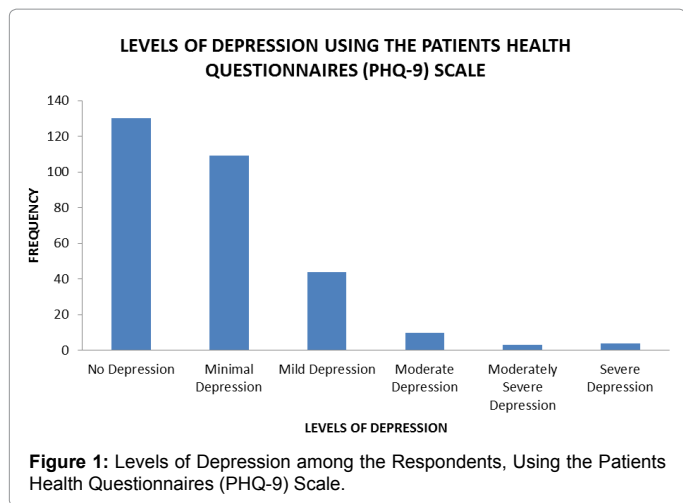


Figure 1: Levels of Depression among the Respondents, Using the Patients Health Questionnaires (PHQ-9) Scale.

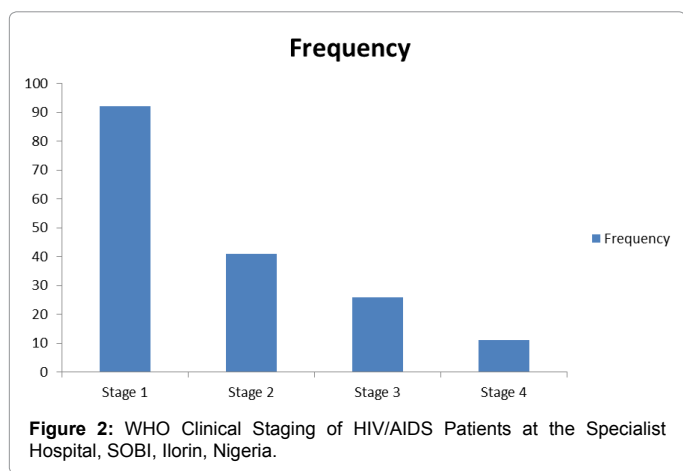


Figure 2: WHO Clinical Staging of HIV/AIDS Patients at the Specialist Hospital, SOBI, Ilorin, Nigeria.

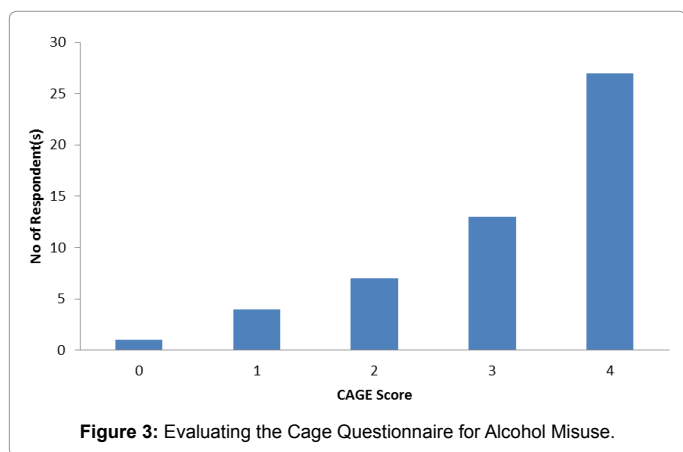


Figure 3: Evaluating the Cage Questionnaire for Alcohol Misuse.

Discussion

The socio demographic factors of gender, age, marital status, education, and income have consistently been identified as important factors in explaining the variability in the prevalence of depression and level of adherence.

The study found a female preponderance, 81.8%. this is consistent with the UNAIDS/WHO global report which stated that unlike women

Drugs	Frequency	Percentage (%)
Cotrimoxazole (Septrin)	52	30.6
Loperamide	37	21.8
Loratidine	29	17.1
Artemether-Lumefantrine	18	10.6
Amoxicillin	13	7.6
Acyclovir	9	5.2
Nystatin	8	4.7
Fluconazole	4	2.4
Total	170	100

Table 3: Opportunistic Infection Medicines at the Specialist Hospital, SOBI, Ilorin, Nigeria.

Drugs	Frequency	Percentage (%)
Rashes	47	27.6
Itching	32	18.8
Headache	28	16.5
Dizziness	17	10.0
Diarrhea	13	7.6
Vomiting	12	7.1
Peripheral Neuropathy	10	5.9
Chest pain	8	4.7
Anaemia	3	1.8
Total	170	100

Table 4: Antiretroviral and Opportunistic Medication Side Effects.

Response	Yes (%)	No (%)	Total
Difficulty in paying travel expenses	62 (36.5)	108 (63.5)	170 (100.0)
Difficulty in paying for registration at the clinic	16 (9.4)	154 (90.6)	170 (100.0)
Losing income as a result of coming to the clinic	98 (57.6)	72 (42.4)	170 (100.0)
Incurring other cost as a result of taking ART	58 (34.1)	112 (65.9)	170 (100.0)

Table 5: Cost Consideration of Treatment.

Variables (Reasons)	Frequency	Percentage (%)	Rank Order
Forgetfulness	63	37.1	1
Stigmatization	31	18.2	2
Being away from home	19	11.2	3
Running out of pills	14	8.2	4
Busy schedule	12	7.1	5
Distance to the clinic	11	6.5	6
Fear of side effects	9	5.3	7
High pill burden	7	4.1	8
Absence of symptoms	4	2.3	9
Total	170	100	

Table 6: Reasons for Non-Adherence to Antiretroviral.

Variables	Frequency	Percentage (%)
Adherence	138	81.2
Non-adherence	32	18.8
Total	170	100

Table 7: Self-Report Patient Assessment of Adherence.

Level	Score	Frequency	Percentage (%)
Minimal	<2	103	60.6
Mild	2.0 - 2.49	33	19.4
Moderate	2.50 - 2.99	19	11.2
Severe	≥ 3.0	15	8.8
Total		170	100%

Table 8: Level of Stigma using the Internalized Stigma of Mental Illness Scale (ISMI).

in other regions of the world, African women are considerably more likely at least 1.4 times to be infected with HIV than men. Possible explanations for the female preponderance in this study is that women had their HIV disease detected through routine screening in the ante-natal clinics or when their babies develop HIV-associated illness shortly after birth.

A number of other studies also report a female preponderance [41]. It is however different from Ilyasu and colleagues [42] who reported male preponderance because of their economic advantage over women.

The mean age of the respondents was 39.0 (SD 10.79). This reflects the fact that people are most sexually active between the ages of 18 and 25 years and are likely to acquire the infection during this period. However, symptoms may not become apparent until roughly 10 to 15 years after initial infection, making it more likely for patients to present in their 30s. This is similar to previous finding [41]. Six (2.0%) were students. The implication of this age group is that, youth, the future of Nigeria, should be targeted for HIV interventions.

As opposed to the findings in Canada, depression is more common among those with low educational level. Education is a critical social determinant of health because people with higher levels of education are often healthier than people with lower levels of educational attainment.

About 25 (8.3%) were unemployed. Unemployment leads to impoverishment and psychological stress. This is similar to a study, where depressive features were more common among the unemployed. Depression resulting from unemployment has increased over the years. One hundred and twenty nine (75.9%) was seen in patients with an income level of less than twenty thousand Naira (N20,000), equivalent to (\$125) us dollars, which is the minimum recommended wage by the Federal Government of Nigeria.

The prevalence of depressive disorders among HIV/AIDS patients attending the Highly Active Anti-Retroviral Therapy (HAART) clinic, at the Kwara State Specialist Hospital Sobi, was 57%. Depressive symptomatology in the population, mirrored presentation of depression in other setting [42]. The study replicates previous findings concerning the prevalence of depressive disorders among People Living With HIV/AIDS (PLWHs) patients in Nigeria in particular. It also falls within the rates seen internationally. The prevalence obtained from this study also agrees with local studies [43,44].

There was significant alcohol misused in the study which may directly or indirectly constitute leads to forgetfulness, hence reason for non adherence to antiretroviral.

Patients on zidovudine based regimen and nevirapine based regimen were more tolerable by the patients than stavudine based therapy due to its neuropathy effect. This is inconsistent with the study of Bolton-Moore et al. [45] that more of their patients were on stavudine based therapy compared to zidovudine regimen. Cotrimoxazole, 30.6% was the commonest used drug for opportunistic infection. Some patients may require other drugs to alleviate the symptoms of medication side effects. The commonest side effect was rashes, 27.6% with or without associated itching, 18.8%. Loratidine was therefore used for Pruritic eruption as well as rashes induced by nevirapine. Haematinics were prescribed for these patients to improved appetite for weight gain and to prevent anaemia initiated by zidovudine. Patients need to be advised to take efavirenz an hour after an oily food to reduce nightmares and dizziness.

Forgetfulness was the commonest reasons attributed to non-adherence. Depression can produce cognitive impairment, as depressed subjects have been found to have impaired attention, concentration and memory. In severe cases, they may have a dementia-like syndrome (pseudo-dementia). The consequence is that depressed patients with HIV/AIDS may be more likely to forget using their pills leading to poor medication adherence. HIV-infected subjects in several studies [46] reported "forgetting" as one of the most common reasons for poor adherence to antiretroviral drugs. It is also possible that HIV-associated neuro-cognitive disturbances, which are common and more prominent as the disease advances might be responsible for some of the cases of poor medication adherence reported in this study. Other studies have reported a significantly greater risk of poor adherence to HAART in HIV-infected persons with neurocognitive impairment [47].

In this study, the level of adherence was 81%. Adherence percentage was calculated as the observed number of doses divided by the number of expected tablets taken multiplied by hundred. This figure compares favourably with 80% [19], 85% [18] obtained by other studies. The study had a better adherence level than 23.1% Kano, Nigeria [48], 58% Ivory Coast [49], United States 63% [50]. It is however lower than, South Africa 87.2% [51], Lagos Nigeria 92% [52], at 3 months and 88% at 18 months.

The reasons for improved adherence level in this study was that all the services rendered to these patients were at no cost which includes free, regular and uninterrupted supply of quality antiretroviral (ARV) drugs, medical laboratory tests and financial support. Also, drugs for opportunistic infections and palliative care were all made free for both in and out patients. Rapid improvement in symptoms and signs that brought the patients to the hospital encouraged adherence. No food restriction, proper follow up, monthly adherence counseling were contributing factors to adherence rate.

Studies in this region have all been limited to public stigma whereas little is known about the extent of self-stigma. Using the Internalized Stigma of Mental Illness scale (ISMI) as a measure of their self-stigma, a profound effect was found on drug adherence. Some patients felt embarrassed while taking their medical folders to pharmacy for prescription refill, despite these folders were similar to other patients in the hospital. In agreement with present study, Grierson and co-workers [53], reported that HIV/AIDS patients have difficulties in taking drugs in public and carrying drugs around thereby adversely affecting adherence. Yao et al. [54] in Togo as well as Talam and colleagues [55] in Kenya supported above factors associated with non adherence.

Conclusion

Depression symptoms are associated with poor adherence to antiretroviral medication. Screening for depressive symptoms at the initiation of antiretroviral therapy, should be part of the standard care of HIV infected patients.

Limitation of the Study

There are few limitations of the study that may reduce the generalization of our findings. The relatively small sample may be a potential limitation. Self-reported measures to assess economic status and depressive symptoms were used. These were prone to participant response bias, such as low reported symptoms due to stigma. Moreover, like all cross-sectional studies, it is difficult to establish causal association between independent and dependent variables.

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