Non-adherence to Highly Active Antiretroviral Therapy and Occurrence of Opportunistic Infections among Adult Clients Accessing Care at a Secondary Health Facility in Imo State Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. Author CCN designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors CBD, DII, EOA, BCU and NAA designed the study, managed the literature searches and implementation. All authors read and approved the final manuscript.

Article Information

Original Research Article

ABSTRACT

Background: Non-adherence remains an issue of concern in highly active anti-retroviral therapy (HAART). It has been reported to reduce the immunological benefit of this regimen, while increasing morbidities and mortalities associated with HIV/AIDS.
Objective: To determine the relationships between non-adherence to HAART and occurrence of opportunistic infections (OIs) among adult HIV clients accessing care in a secondary health facility in Imo state Nigeria.
Materials and Methods: This was a health facility-based descriptive cross-sectional study of 350

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respondents, selected by systematic sampling technique. Data were collected by interview using semi-structured questionnaire and analysed with statistical package for social sciences version 22.0. Test of statistical significance was done using chi-square test, while statistical significance was set at p value ≤ 0.05.

Results: Majority 220 (62.9%) of respondents were females, 218 (62.3%) were currently married, 263 (75.1%) attained at most secondary level of education, while 259 (74%) were resident outside the study area. Twenty (5.7%) of them were non adherent to HAART and reasons cited include: fourteen (4%) forgetting to take medicine and 11 (3.1%) drug is out of stock. Fifty seven (16.7%) ever had OIs with oral thrush 21 (36.8%) as the commonest. There was an association between non- adherence to HAART and occurrence of OIs (p=0.000).

Conclusions: This survey found an association between non- adherence to HAART and occurrence of OIs. We recommend interventions that combine early treatment of OIs and gender cum couple targeted behavioral change communication in addressing non-adherence.

1. INTRODUCTION

Adherence to HAART regimen is defined as taking all the prescribed medication at the right time, in the right doses and in the right way [1]. Medication adherence and non-adherence have been estimated with the extent to which a patient/ client takes a medication in accordance or otherwise respectively, with the intent of the prescribing health care provider [2]. The time period used to define adherence to HAART varies from one study to another, within the range of one day to one month [3].

In clinical trials and clinical practice, nonadherence to medications is not uncommon among patients suffering from chronic diseases. The shift to the use of drug combination therapies for treating HIV has led to increasingly complex drug regimens such as HAART [4]. Three classes of drugs constitute HAART regimens [5]. These are: nucleoside analog reverse transcriptase (RT) inhibitors e.g. abacavir, adefovir, Tenofovir disoproxil, zidovudine, non-nucleoside analog RT inhibitors e.g. Efavirenz, Etravirine, Nevirapine, Rilpivirine, and protease inhibitors (PI) e.g. atazanavir, darunavir, fosamprenavir, nelfinavir, ritonavir, saquinavir.

It has been documented that OIs are important causes of morbidities and mortalities in persons living with HIV/AIDS (PLWHA) [6]. This is because HIV related immunological dysfunction limits the hosts' defences against opportunistic pathogens and thus enhances spread of HIV [7]. These OIs include: recurrent bacterial infections caused by encapsulated germs (Haemophilus influenzae, Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pneumoniae), Cerebral toxoplasmosis, Contagious molluscum, Cryptococcus neoformans infection, Cryptosporidium parvum, cytomegalovirus infection, disseminated Mycobacterium avium complex, esophageal candidiasis, hepatitis C, nocardiosis, Pneumocystis jirovecii pneumonia, progressive multifocal leucoencephalophy. extrapulmonary, ganglionar and pulmonary tuberculosis, simple herpes infection, varicella-zoster and visceral leishmaniasis.

While the main purpose of HAART is to prevent these HIV-related indicators such as morbidities and mortalities, its potential for long-term effectiveness depends on the extent to which the regimen suppresses HIV replication [2]. The HAART also increases the number of CD4 lymphocytes and improves their function, re-establishing the defences of the host and improving chances of host survival [4,8]. This aim can hardly be achieved, even with minimal non-adherence. In other words, non-adherence to HAART regimen presents significant challenges to both clients and health-care providers. Previous studies have supportive evidence on strong correlation between adherence and clinical outcomes [4,9,10]. Nonetheless after CD4 count, antiretroviral adherence has been rated the second strongest predictor of progression to AIDS as well as chance of survival or death [11,12]. Also, non-adherence has been linked with increase in the risk of therapy failure and drug resistance [13,14,15,16].

In the absence of an effective vaccine or curative therapy for HIV/AIDS, prolonging survival of PLWHA implies taking drugs for life. Non-adherence continues to be a major barrier to successful treatment with HAART for PLWHA

[15,17]. It remains a priority area in public health research. To our knowledge, no previous studies have been conducted in our study area on the relationships between non-adherence to HAART and occurrence of OIs, if any. It is expected that our study findings would help in bridging the knowledge gaps that presently exist. Thus the index study was conducted to determine the relationships between non-adherence to HAART and occurrence of OIs among adult HIV clients accessing care in a secondary health facility in Imo state Nigeria.

2. MATERIALS AND METHODS

2.1 Study Area, Period and Design

This health facility based cross-sectional descriptive study was conducted from June to December 2015 at the General Hospital Awo Omamma. Awo Omamma is the headquarters of Oru East local government area (LGA) in Imo state, Nigeria. According to the 2006 National Population Census, the LGA had an estimated population of 111,822 people. The Hospital is the only nodal center in the entire LGA, with 3372 registered adults living with HIV/AIDS. This center is managed by various cadre of health workers, has the relevant resources for CD4 count estimation, counselling sessions and regular check-ups, and provides HAART free of charge. According to the March 2015 monthly report of this ART center, the HIV clinic runs on Tuesdays and Thursdays from 8am to 4pm with an average attendance of 93 clients per clinic day.

2.2 Study Population and Sampling Technique

The target population consisted of the HIV positive clients accessing care at the General Hospital Awo Omamma. Clients aged 18 years or older, registered, who had been on HAART for at least six months prior to this study, were included. Clients who were unable to communicate (e.g. deaf and dumb), were seriously ill, and did not consent to participate in the study were excluded.

The Leslie Kish's formula for single proportions in populations greater than 10,000 was used, which stated [18]: $n = Z^2pq/d^2$ where, n = minimum sample size estimated; Z = standard normal deviate set at 1.96 which corresponds to 95% confidence interval [CI], p= prevalence of non-adherence to anti-retroviral drug, while q=1-p

and d = level of precision usually set at 0.05. According to the World Health Organization, non-adherence to HAART in developing countries is 20% to 40% [19]. Assuming an average of 30% non-adherence, i.e. p=0.3 and q=0.7, the total sample size required was calculated to be 323 clients.

Then a conversion was made using the formula for the calculation of minimum sample size in populations less than 10,000, [18] nf = n/1 +n/N, where N = target population = 3372, and nf = 295 clients. Anticipating a response rate of 90%, an adjustment of the sample size estimate to cover for non- response rate was made by dividing the sample size estimate with a factor f, i.e. n/1-f, where f is the estimated response rate[18].Thus the calculated sample size =295/0.9 = 328 clients. However, 350 questionnaires were administered.

Systematic random sampling technique was used to conduct this study as follows: Complete enumeration method was adopted with the clinic register used as the sampling frame. A sampling fraction was determined by dividing the number of clients booked for appointment on each data collection day by the minimum number of clients to be interviewed. Based on this, every n[th] eligible consenting client presenting for care was enrolled into the present study and interviewed consecutively and in private, until the target sample size was attained.

2.3 Data Collection and Analysis

Pre-tested, interviewer-administered semi-structured questionnaires. The questionnaire for this study was adapted from relevant literature. HAART-related profiles of the clients were taken from ART cards and medical records. The information obtained through the interviews was checked and verified by pill-count. If a client missed a single dose of HAART out of the total eight doses within a four-day schedule, the client's adherence would be < 95% [20,21]. In this study, non-adherence is defined as a self-report of missing at least a single dose of medication over the previous four days.

To ensure data quality, training of data collection team, field monitoring of data collection was done. Meeting of data collection team at the end of every day to share experiences, submit completed forms and solve field problems was ensured. The data were reviewed, entered into the computer and were cleaned by carrying out

range and consistency checks. Descriptive and analytical statistics of the data were carried out using statistical package for social sciences (SPSS) Windows version 22.0 [22]. Descriptive data were presented as simple frequencies and percentages. Frequencies of the variables were assessed using univariate analysis, while bivariate analysis using chi-square test determined associations between different socio-demographic and clinical variables in relation to nonadherence to HAART. Level of significance was set at 5% or less.

3. RESULTS

Table 1 shows the socio- demographic characteristics of respondents. A total of 350 questionnaires were distributed, all of which were filled and thus analysed. This gives a response rate of 100%. The modal age group of respondents was 30-39 years. Majority of respondents 220 (62.9%) were females, 218 (62.3%) were currently married, 327 (93.4%) were Christians, 263 (75.1%) attained at most secondary level of education, 191 (54.6%) were traders, 314 (89.7%) were Ibos while 259 (74%) were resident outside the study area.

Table 2 highlights non-adherence to HAART, reasons for non-adherence, and CD4 count of respondents. Twenty (5.7%) of the respondents were non adherent to HAART, while reasons for non-adherence to HAART include: fourteen (4%) forgetting to take medicine, 11 (3.1%) drug is out of stock/ unavailable and 11 (3.1%) busy schedule. One hundred and fifty seven (44.9%) had CD4 count ≥500 cells/µL.

Table 3 summarizes the occurrence of opportunistic infections among respondents. Fifty seven (16.7%) ever had OIs, while types of OIs suffered include: twenty one (36.8%) oral thrush, 12 (21.1%) tuberculosis, 12 (21.1%) genital candidiasis.

Table 4 shows the relationship between non-adherence to HAART and Occurrence of opportunistic infections among respondents. There was a statistically significant association between non- adherence to HAART and occurrence of OIs among respondents ($\chi2$ = 23.3196, p=0.000).

4. DISCUSSION

This was a cross-sectional study designed to determine the relationships between non-adherence to HAART and occurrence of OIs

among adult HIV clients accessing care in a secondary health facility in Imo state Nigeria, where HAART is dispensed free of charge.

The index study reported that there were at least six females in every ten respondents. This female predominance could be linked to the feminization of HIV/AIDS, a phenomenon that has been used to explain the gender variation of increase in burden of HIV in females compared to their male counterparts. This trend is often blamed on cultural norms that limit women's access to information about HIV prevention, fear of violence, economic dependence among women and inter-gender power imbalance that makes it difficult for women to negotiate safe sexual practices with their partners. Higher care seeking behavior reported among women compared to their male folks, could proffer an alternative explanation to this finding. This is consistent with findings of the 2012 National HIV/AIDS and Reproductive Health Survey (NARHS) conducted by the Nigerian Federal Ministry of Health also reported a higher prevalence of HIV in females [23] and several other studies in Nigeria [24,25,26].

Our results revealed that most (93.4%) of the respondents were currently married. Bello et al., in a study of HIV/AIDS clients in a secondary health care facility in Ilorin Nigeria also reported a preponderance of the currently married [24]. This higher proportion of currently married respondents could be explained by the position that currently married HIV positive individuals especially those in concordant partnerships, may feel less stigmatized accessing care compared with their not married counterparts, who may feel more stigmatised because of fears such as that of losing possible partners [23].

From our study findings, about three-quarters of respondents were resident outside the study area. This picture could still be explained in the line of stigmatisation as a result of which some PLWHA do not want to be seen accessing HIV care and services in their own domicile. They would rather journey to far away centers even in states outside their place of residence to access care, mainly to protect their privacy. There is need to strengthen the capacity of health system via policies, legislation and other measures that could boost behavioral change, significantly check stigmatisation and thus improve access cum adherence to HAART among clients.

Our results revealed a low level of nonadherence (5.7%) to HAART, among adult PLWHA. This is

in keeping with the findings reported in other studies e.g. 6.5% in South Africa [27], 5%–7% in Senegal [28] where it was also noted that clients receiving HAART free of charge were found to have a higher adherence to HAART than paying clients. In the present study, reasons for non-adherence to HAART include: forgetting to take medicine, drug is out of stock/ unavailable and busy schedule. This finding is in tandem with that of several studies [29,30,31].

Table 1. Socio- demographic characteristics of adult clients accessing care at a secondary health facility in Imo state Nigeria from June to December 2015

Characteristics	Frequency N=350	Percentage (%)
Age(years)		
18-19	19	5.4
20-29	39	11.1
30-39	135	38.6
40-49	88	25.1
50-59	45	12.9
60-69	17	4.9
> 70	7	2
Gender		
Male	130	37.1
Female	220	62.9
Marital status		
Never married	78	22.3
Currently married	218	62.3
Widowed	44	12.6
Divorced	5	1.4
Separated	5	1.4
Religion		
Christianity	327	93.4
Islam	20	5.7
Traditional	3	0.9
Highest educational level		
Nil formal	14	4
Primary	78	22.2
Secondary	171	48.9
Tertiary	87	24.9
Occupation		
Trading	191	54.6
Civil servant	72	20.6
Student	41	11.7
Artisanship	18	5.1
Driving	11	3.1
Unemployed	18	3.1
Ethnicity		
Hausa.	15	4.3
Ibo	314	89.7
Yoruba.	18	3.1
Others*	3	8.6
Residence		
Within the community	91	26
Outside the community	259	74

* Others- , Efik, Igala, Ijaw.

Table 2. Non adherence to HAART, reasons for non-adherence, and CD4 count of adult clients accessing care at a secondary health facility in Imo state Nigeria from June to December 2015

Variables	Frequency N=350	Percentage (%)
Non-adherence to HAART		
Yes	20	5.7
No	330	94.3
Total	**350**	**100**
Reasons for non-adherence*		
Forgetting to take medicine	14	4
Drug is out of stock/ unavailable	11	3.1
Busy schedule	11	3.1
Fear of side effects	10	2.9
Felt I have been cured of the disease	5	1.4
CD4 cell count categories (cells/μL)		
≥500	157	44.9
200-499	134	38.2
<200	59	16.9
Total	**350**	**100**

* Multiple responses

Table 3. Occurrence of opportunistic infections among adult clients accessing care at a secondary health facility in Imo state Nigeria from June to December 2015

Variables	Frequency	Percentage (%)
Ever had opportunistic infection (n=350)		
Yes	57	16.2
No	293	83.8
Total	**350**	**100**
Type of opportunistic infections suffered, (n=57)		
Oral thrush	21	36.8
Tuberculosis	12	21.1
Genital candidiasis	12	21.1
Genital warts	7	2
Kaposi sarcoma	5	1.4

Table 4. The relationship between non- adherence to HAART and Occurrence of opportunistic infections among adult clients accessing care at a secondary health facility in Imo state Nigeria from June to December 2015

Variables	Occurrence of opportunistic infections			Test statistic	p value
	Frequency/percentage %			χ^2	
	Yes (%)	No (%)	Total (%)		
Non-adherence to HAART					
Yes (%)	11 (3.1)	9 (2.6)	20 (5.7)		
No (%)	46 (13.1)	284 (81.2)	330 (94.3)	23.3196	0.000*
Total (%)	**57 (16.2)**	**293 (83.8)**	**350 (100)**		

* Statistically significant association = $p \leq 0.05$

The present study also reported that (16.7%) ever had OIs, while types of OIs suffered include: oral thrush, tuberculosis, genital candidiasis. Though our study did not classify occurrence of OIs into pre- HAART, early HAART and late HAART, as in the study by Rubaihayo, et al., in Uganda, tuberculosis and candidiasis also ranked tops in frequency of OIs suffered by these clients [32]. Similar OIs were also reported in studies in Nigeria and other resource poor African settings [33,34,35,36]. This might be because these OIs are highly endemic in the region and has simple diagnostic procedures too.

The current research bivariate analysis revealed a statistically significant association between non- adherence to HAART and occurrence of OIs among respondents. Previous studies have supportive evidence on strong correlation between adherence and clinical outcomes such as occurrence of OIs, especially among HIV positive patients in resource poor settings [9,10,37,38,39,40]. Occurrence of OIs could thus be a challenge to the attainment of the sustainable development goal (SDG) three on health in these resource poor settings.

5. LIMITATIONS AND STRENGTH OF THE STUDY

Firstly, studies based on self-reports reflect only short-term or average adherence and may often overestimate it. This could affect the validity and reliability of the results. Thus the information obtained through the interviews was checked and verified by pill-count. However, pill counts require clients to return the medication packaging to the clinician. Even in clinical trial situations, clients tend to forget the packages or inadvertently discard them. Assurance of confidentiality of the respondents, the training of research assistants to be painstaking in answering possible questions raised by respondents during data collection and the simple and direct nature of the questions reduced these effects. Also, to avoid recall bias, a short period of history (four days) was used for measuring non-adherence in the present study. A major strength of this study is the 100% response rate obtained.

6. CONCLUSIONS

In this study, the researchers examined the relationships between non-adherence to HAART and occurrence of OIs among adult HIV clients. Results from the current study showed that majority of the clients were females, currently married and resident outside the study area. There was a low level of non-adherence to HAART and the key reasons for non-adherence to HAART include: forgetting to take medicine, drug is out of stock/ unavailable and busy schedule. About (16.7%) ever had OIs, while types of OIs suffered include: oral thrush, tuberculosis, genital candidiasis. And there was a statistically significant association between non-adherence to HAART and occurrence of OIs among respondents.

Although overall non-adherence was low, addressing non-adherence with proper counselling and motivation of clients may provide valuable information about how non-adherence could be curbed. We also recommend comprehensive gender cum couple targeted behavioral change communication, reinforcing positive living by tailoring of the drug regimen to the lifestyle of the clients, and assessing adherence as part of a follow-up program.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/20946