



# Adverse Drug Effects and Non-Adherence to Antiretroviral Therapy in Nigeria: A Review

Mary Obidiya Okuku<sup>1\*</sup> and Alali Dan-Jumbo<sup>1</sup>

<sup>1</sup>Infectious Disease Unit, Rivers State University Teaching Hospital, Port Harcourt, Nigeria.

## Authors' contributions

This work was carried out in collaboration between both authors. Both authors prepared and wrote the review. Both authors read and approved the final manuscript.

## Article Information

DOI: 10.9734/AJARR/2021/v15i130354

Editor(s):

(1) Dr. Fagbadebo Omololu Michael, Durban University of Technology, South Africa.

Reviewers:

(1) Shikha Gulati, University of Delhi, India.

(2) Jesús Enrique Pérez Bastán, Cuba.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/64746>

**Received 06 November 2020**

**Accepted 12 January 2021**

**Published 28 January 2021**

Review Article

## ABSTRACT

**Objectives:** This review aims to assess the link between adverse drug effects and non-adherence to antiretroviral therapy (ART) among people living with HIV/AIDS (PLWHA) in Nigeria.

**Methodology:** Databases were searched namely PubMed, Web of science core collection, Science direct, Global Health (CABI) and MEDLINE. Fifteen (15) primary articles (studies carried out in Nigeria) met the inclusion criteria and were selected for the review. The primary articles selected for the review were analyzed and critiqued.

**Results:** The articles selected for review showed that adverse drug effects is a barrier to adherence to ART.

**Conclusion:** The review conclude that adverse drug effect is a barrier to adherence to ART among PLWHA in Nigeria and recommends patient education on side effects of ART, the need for regular exercises, eating healthy meals and the need for physicians to simplify the regimen with regards to the amount of medication to take and the timing.

**Keywords:** Side effects; adverse effects; non-adherence; antiretroviral; HIV/AIDS; Nigeria.

\*Corresponding author: Email: maryokuku@yahoo.com;

## 1. INTRODUCTION

The WHO [1] defined adverse drug reaction as “a response which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis, or therapy of disease, or for modification of physiological function”. PLWHA most times need antiretroviral drug combinations (3 to 4) and adherence is an important factor in prevention of treatment failure [2].

In their study, [3] argued that in resource-limited countries that HIV treatment failure is caused by adverse drug reactions and drug intolerance. They also maintained that this non-adherence causes the transmission of drug-resistant viruses, rise in morbidity, mortality, treatment failure and increased hospitalization.

A clinical trial by [4] argued that there is a striking association between virological suppression and drug adherence in HIV infection treatment. Other studies have shown that ART causes different adverse effects which could be long term or short term effects and hinders the patients from adhering to their medication regimen [5,6]. These analysts maintain that patients experience different types of ART adverse drug reactions and some examples are below.

### 1.1 Short Term Adverse Drug Effect of Art

This includes headache, tiredness, vomiting, diarrhea, fever, muscle pain and sleeplessness [5,6,7].

### 1.2 Long Term Adverse Drug Effect of ART

Includes liver damage, heart disease, osteoporosis (weakening of the bones), nerve damage, mental health problems such as suicidal thoughts and depression [5,6,7].

This review aims to assess the link between adverse drug effects and non-adherence to antiretroviral therapy (ART) among people living with HIV/AIDS (PLWHA) in Nigeria. For the purpose of this review, studies on adults only will be analyzed.

## 2. METHODOLOGY

Databases were searched comprehensively namely PubMed, Web of science core collection, Science direct, Global Health (CABI) and

MEDLINE to identify studies on non-adherence to ART in Nigeria. The inclusion criteria include: all adults 19 years plus, articles written from 2009 to 2020, peer reviewed journals, primary articles, articles written in English and Ovid full text available journals. Systematic reviews, secondary articles, unpublished articles, pregnant women, children, infants, age below 19 and articles written in other languages other than English were excluded from the study. Fifteen (15) primary articles met the inclusion criteria and were selected for the review. The primary articles selected for the review were analyzed and critiqued.

## 3. RESULTS AND DISCUSSION

Looking at Table 1, the 15 primary articles selected for this study suggests that adverse drug effects are barriers to adherence to ART among PLWHA in Nigeria. However, the degree of non-adherence due to adverse drug effects varied in the studies as shown on Table 1. Studies [8] and [9] had the lowest figures 1.3% and 2.4% non-adherence rate out of 461 and 411 participants respectively.

The study by [8] had the lowest percentage at 1.3% (out of 461 participants) non-adherence to ART due to side effects. They reported that the participants received varying ART doses ranging from three times a day, twice a day and once a day dosing. One may argue that the patients may have received a convenient and a dosing regimen with minimal side effects leading to the reduced percentage seen in Table 1.

About 4.2% of 282 of the study population in [10] reported adverse drug effects as the reason for their non-adherence to ART. The study did not explore further factors that influenced the non-adherence nor state the side effects the patients experienced.

Suleiman and Momo [11] reported 5.5% of non-adherence linked to adverse drug effects in a population size of 601 in their study. They stated that about 58.9% (354) of the patients were on one tablet twice daily medication regimen (triple combination). While about 24.8% (149) of the patients were on once daily triple combination regimen. This suggests that the patients had less medications to take and their dosing times were well spaced. This could be the reason they had less number of persons reporting adverse drug reactions as reason for non-adherence to ART.

**Table 1. Fifteen primary articles that reported adverse drug effects as a barrier to adherence to art in Nigeria**

s/n	Authors	Number of participants	Adverse effect % (percentage of persons who linked their non-adherence to ART to adverse drug effects)
A	Falang, Akubaka and Jimam [8]	461	1.3
B	Oku et al. [9]	411	2.4
C	Onyeonoro et al. [10]	282	4.2
D	Suleiman and Momo [11]	601	5.5
E	Nduaguba et al. [12]	361	5.8
F	Bello [13]	213	6.6
G	Muoghalu [14]	200	7.0
H	Agu et al. [15]	118	7.7
I	Odili, Obiechie and Amibor [16]	300	8.7
J	Chineke et al. [17]	400	9.3
K	Pennap, Abdullahi and Bako [18]	250	14.5
L	Okoronkwo et al. [19]	221	31.9
M	Olowookere et al. [20]	318	35.2
N	Anyaike et al. [21]	550	66.7
O	Uzochukwu et al. [22]	174	76.3

The study by [12] recorded 5.8% non-adherence to ART due to adverse drug effects among 361 participants. They also reported that the nurses in the facility where the study was conducted did home visits and delivered the patients medications to them at home whereas the other studies on Table 1 did not report this. This implies that there may have been a regular follow-up of the patients by the nurses and with that the nurses will likely counsel and monitor patients' ART intake which if patients adheres to will minimize the adverse effects experienced.

Additionally, the study by [13] had a 6.6% (out of 213 participants) non-adherence to ART due to side effects. They reported that the participants in the study received free medications for the treatment of opportunistic infections and also received free palliative care both as out and in patients. This shows that the patients' health received constant checks which may have averted the side effects of ART which may have arisen. Hence, the low percentage reported.

Moughalu [14] reported 7.0% of adverse drug effect among the 200 patients studied. The side effects of ART reported by the patients include body weakness and frequent urination. However, the study did not specify the role of the medical personnel that may have contributed to the reduction in the percentage of the side effect reported.

Furthermore, [15] had 7.7% (out of 118 participants) non-adherence to ART due to side

effects. They maintained in their study that the participants had good rapport with their healthcare providers. This suggests that patients' close relationship with his/her healthcare providers could promote close monitoring as there is a likelihood that the healthcare provider will always keep in touch with patients and can easily advise and give guidance on any complaint by the patient in the course of the treatment.

The study by [16] recorded 8.7% of non-adherence to ART due to adverse drug effects among 300 patients. The study reported loss of appetite, cough, skin rashes, body weakness, fainting, headaches and watery stool as the side effects reported by the patients. However, the study reported that about 5% of the patients had other diseases. It could be argued that these side effects experienced by these patients may not be due to ART intake but could be due to this other diseases they have.

According to [17] and [18], they had 9.3% and 14.5% of non-adherence to ART due to adverse drug effects in a population of 400 and 250 patients respectively. While [17] reported skin rashes as side effect of ART reported by their patients, [18] did not specify the adverse drug reactions the patients experienced, but advised that healthcare professionals should educate patients on the side effects they may experience as this will help them not to stop the medications despite the side effects.

The study by [19] had 31.9% (out of 221 participants) of non-adherence to ART due to adverse drug effects. But the surprising thing is that they reported that the participants were followed up monthly. It is really not clear why despite the monthly follow-up the participants still recorded a high percentage of persons who experienced adverse drug effects.

According to [20] which had 35.2% rate of non-adherence to ART due to adverse drug effects in their study, the side effects reported by the patients were nausea, vomiting, diarrhea, skin rashes, paresthesia, dizziness and bad dreams. This made them to discontinue their ART. Most PLWHA have comorbidities and other diseases. Hence, healthcare professionals need to do proper investigations to determine the actual cause of the side effects reported by PLWHA.

While [21] and [22] recorded the highest rate of non-adherence due to adverse drug effects at 66.7% and 76.7% out of 500 and 174 participants respectively. [21] argued that ascertaining the specific side effects experienced by the patients was difficult as the self-report given by these patients may have had some element of bias. In other words, there is a possibility that the patients may have provided a socially acceptable answer due to the sensitivity of the questionnaires thus providing incomplete responses. With the varying figures as seen on Table 1, more research is needed to ascertain the reasons why there are varied percentages of adverse drug effects in the studies.

Other studies in other countries also maintain that adverse drug effects are a barrier to adherence to ART. For instance, [23] in their study of 556 Italian Cohort treatment naive HIV patients on ART to discover reasons for discontinuation of ART among them, reported that within the first 12 months of their follow-up period of 45 weeks, 148 of the patients (21.1%) stopped taking combination ART as a result of treatment toxicity. A similar study by [24], a cross-sectional HIV Epidemiology Research Cohort study maintained that individuals who experienced two or more side effects of ART were more probable to stop treatment compared to those who did not experience any side effect of ART.

Furthermore, [25] in their French cohort study of HIV positive patients to determine factors responsible for non-adherence to ART argued that patients' discontinuation of ART was

attributed to the adverse drug effect the patients experienced. They further emphasized that for every additional adverse drug effects patients' experienced, that there was a high probability of a rise of about 95% (1.13) confidence interval (accuracy of an estimate) of the odds of non-adherence.

Although it could be argued that [23,24,25] studies were carried out a long time and there is likelihood of their conclusions being different now regarding the relationship between adverse drug reaction and ART adherence. However, more recent studies support their various conclusions. A prospective observational study (2 months follow up) conducted by [26] among 327 HIV positive patients in India, to assess the types, incidence and nature of adverse effects of ART on them revealed that 43 of the participants developed adverse drug effects which made them stop taking their ART.

Similarly, a cross-sectional survey in Iran from 2009 to 2010 conducted by [27] among 200 patients who were HIV positive to find out the prevalence of adverse drug reactions among them while they take their ART. The result showed that 188 of the participants experienced diverse side effects of ART which led to reduced adherence to therapy while some discontinued treatment. Furthermore, a systematic review and qualitative meta-synthesis by [28] to assess the influence of antiretroviral side effects to its adherence discovered that out of the 39 articles identified for the review, 33 concluded that ART adverse effect causes reduced adherence to therapy.

According to [29] systematic reviews findings are credible as it undergoes transparent and rigorous approach in collation of its evidence and data analysis, promoting the drawn conclusions scientific standing. In other words, these studies confirm that adverse drug reaction is a barrier to adherence to ART among PLWHA and should be given attention in order to curtail the side effects they experience and promote their adherence. Hence, the need for healthcare professionals to find solutions to reduce the effect of adverse drug reactions.

With regards to the possible solutions to minimize adverse drug reactions, patient education is vital so that they understand these adverse drug reactions and know what to expect before initiation of therapy or changing of therapy. The study by [6] discussed that

participants who were counseled on the possible adverse effect of ART were able to cope with the side effects and that did not affect their adherence.

The study by [30] and [31] maintained that patients should be taught to adopt some coping strategies such as:

- Resting and copious fluid intake to combat dizziness.
- Snacking or eating a meal to control nausea.
- Exercise to reduce / remove building up of unwanted fat deposits in the body.
- Reduction of intake of dairy food, fatty, spicy and fried food to prevent diarrhea.
- Avoiding smoking and alcohol intake, and eating nutritious meals to reduce fatigue.
- For skin rashes, wearing long sleeve clothes and ankle reaching trousers or skirts to hide the sores.

#### 4. CONCLUSION

This review concludes that adverse drug effects is a barrier to non-adherence to ART among PLWHA in Nigeria. Patient education by healthcare professionals is vital as patients need to understand the importance of always going for routine medical checkup. This will enable early detection of any underlying disease which could also be a hindrance to their following and keeping to their ART regimen. If patients receive appropriate adherence counseling and have knowledge of all these, they will be able to cope with the adverse drug reactions and can adopt appropriate preventive measures to combat it.

#### 5. LIMITATIONS

The studies did not classify / specify the age or gender that reported adverse drug effects as the reason for non-adherence to ART. Some did not also specify or mention the specific adverse effects reported by the patients. More research is needed to ascertain these factors.

#### CONSENT

It is not applicable.

#### ETHICAL APPROVAL

It is not applicable.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

#### REFERENCES

1. World Health Organisation. Surveillance of antiretroviral drug toxicity during pregnancy and breastfeeding. Geneva: World Health Organisation; 2015.
2. Rajesh R, Sudha V, Varma DM, Sonika S. Association between Medication Adherence Outcomes and Adverse Drug Reactions to Highly Active Antiretroviral Therapy in Indian Human Immunodeficiency Virus-Positive Patients. *J Young Pharm.* 2012;4(4):250-260.
3. Rajesh R, Vidyasagar S, Patel N, ManjuVarghese J. Safety Aspects of Antiretroviral Therapy for Management of HIV Infection. *J Basic Clin Pharm.* 2009; 1(1):47-53.
4. Mannheimer S, Friedland G, Matts J, Child C, Chesney M. The consistency of adherence to antiretroviral therapy predicts biologic outcomes for human immunodeficiency virus-infected persons in clinical trials. *Clin Infect Dis.* 2002;34(8): 1115-21.
5. Nadkar MY, Bajpai, S. Antiretroviral therapy: toxicity and adherence. *Journal of the Association of Physicians of India.* 2009;57:375-376.
6. Torres TS, Cardoso SW, Velasque LS, Veloso VG, Grinsztejn B. Incidence rate of modifying or discontinuing first combined antiretroviral therapy regimen due to toxicity during the first year of treatment stratified by age. *The Brazilian Journal of Infectious Diseases.* 2014;18(1):34-41.
7. Chesney M. Adherence to HAART regimens. *AIDS Patient Care and STDs.* 2003;17(4):169-177.
8. Falang KD, Akubaka P, Jimam NS. Patient factors impacting antiretroviral drug adherence in a Nigerian tertiary hospital. *Journal of Pharmacology and Pharmacotherapeutics.* 2012;3(2):138-142.
9. Oku AO, Owoaje ET, Ige OK, Oyo-ita A. Prevalence and determinants of adherence to HAART amongst PLHIV in a tertiary health facility in south-south Nigeria. *BMC Infectious Diseases.* 2013;13(401):1471-2334.
10. Onyeonoro UU, Ebenebe UE, Ibeh CC, Nwamoh UN, Ukegbu AU, Emelumadu

- OF. Adherence to antiretroviral therapy among people living with human immunodeficiency virus / acquired immunodeficiency syndrome in a tertiary health facility in South Eastern Nigeria. *Journal of HIV & Human Reproduction*. 2016;1(2):58-62.
11. Suleiman IA, Momo A. Adherence to antiretroviral therapy and its determinants among persons living with HIV/AIDS in Bayelsa state, Nigeria. *Pharmacy Practice*. 2016;14(1):631-637.
  12. Nduaguba SO, Soremekun RO, Olugbake OA, Barner JC. The relationship between patient-related factors and medication adherence among Nigerian patients taking highly active anti-retroviral therapy. *African Health Sciences*. 2017; 17(3):738-745.
  13. Bello SI. HIV/AIDS Patients' Adherence to Antiretroviral Therapy In Sobi Specialist Hospital, Ilorin Nigeria. *Global Journal of Medical Research*. 2011;11(2):17-26.
  14. Muoghalu CO. Factors influencing adherence to anti-retroviral therapy among people living with HIV/AIDS attending the State Hospital, Osogbo, Nigeria. *HIV & AIDS Review*. 2018;17(4):288-298.
  15. Agu KA, Okojie O, Oqua D, King RC, Omonaiye O, Onuoha C, Isah MA, Iyaji PG. Medication Adherence and Risk Factors for Non-adherence Among Patients Taking Highly active Antiretroviral Therapy. *West African Journal of Pharmacy*. 2011;22(1):19-26.
  16. Odili VU, Obieche AO, Amibor KC. Adherence to Antiretroviral Therapy and Its Determinants Among HIV-Infected Patients in Nigeria. *Journal of Pharmacy Practice*. 2017;30(3):291-295.
  17. Chineke HN, Adogou POU, Uwakwe KA, Ewuzie MU. Assessment of level of Adherence to Antiretroviral Therapy among Human Immune Deficiency Virus/acquired Immune Deficiency Syndrome Patients at Imo State University Teaching Hospital, Orlu, Nigeria. *Nigerian Journal of General Practice*. 2015;13(1):21-25.
  18. Pennap GR, Abdullahi U, Bako IA. Adherence to highly active antiretroviral therapy and its challenges in people living with human immunodeficiency virus (HIV) infection in Keffi, Nigeria. *Journal of AIDS and HIV Research*. 2013;5(2):52-58.
  19. Okoronkwo I, Okeke U, Chinweuba A, Iheanacho P. Nonadherence Factors and Sociodemographic Characteristics of HIV-Infected Adults Receiving Antiretroviral Therapy in Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria. *ISRN AIDS*. 2013;2013(2013):1-8.
  20. Olowookere SA, Fatiregun AA, Akinyemi JO, Bamgboye AE, Osagbemi GK. (2008) Prevalence and determinants of nonadherence to highly active antiretroviral therapy among people living with HIV/AIDS in Ibadan, Nigeria. *Journal of Infection in Developing Countries*. 2008;2(5):369-372.
  21. Anyaike C, Atoyebi OA., Musa OI, Bolarinwa OA., Durowade KA, Ogundiran A, Babatunde OA. Adherence to combined Antiretroviral therapy (cART) among people living with HIV/AIDS in a Tertiary Hospital in Ilorin, Nigeria. *Pan African Medical Journal*. 2019;32(10):1-12.
  22. Uzochukwu BSC, Onwujekwe OE, Onoka AC, Okoli C, Ugwu NP, Chukwuogo OI. Determinants of non-adherence to subsidized anti-retroviral treatment in Southeast Nigeria. *Health Policy and Planning*. 2009;24(3):189-196.
  23. Mocroft A, Youle M, Moore A, Sabin CA, Madge S, Lepri AC, Philips AN. (2001) Reasons for modification and discontinuation of antiretroviral: Results from a single treatment centre. *AIDS*. 2001;15(2):185-194.
  24. Stone VE, Hogan JW, Schuman P, Rompalo AM, Howard AA, Korkontzelou C, Smith DK. Antiretroviral regimen complexity, self-reported adherence, and HIV patients' understanding of their regimens: Survey of women in the HER study. *Journal of Acquired Immune Deficiency Syndrome*. 2001;28(2):124-131.
  25. Duran S, Spire B, Raffi F, Walter V, Bouhour D, Journot V, APROCO Study Group. Self-reported symptoms after initiation of a protease inhibitor in HIV-infected patients and their impact on adherence to HAART. *HIV Clinical Trials*. 2001;2(1):38-45.
  26. Jha AK, Gadgade A, Shenoy AK, Chowta MN, Ramapuram JT. Evaluation of adverse drug reactions in HIV positive patients in a tertiary care hospital. *Perspectives in Clinical Research*. 2015;6(1):34-38.
  27. Koochak HE, Babaii A, Pourdast A, Golrokhy R, Rasoolinejad M, Khodaei S, Moghadam SRJ, Taheri RR, Seyed ASA. Prevalence of Adverse Drug Reactions to Highly Active Antiretroviral Therapy (HAART) among HIV Positive Patients in

- Imam Khomeini Hospital of Tehran, Iran. Infectious Disorders Drug Targets. 2017;17(2):116-119.
28. Li H, Marley G, Ma W, Wei C, Lackey M, Ma Q, Renaud F, Vitoria M, Beanland R, Doherty M, Tucker JD. The Role of ARV Associated Adverse Drug Reactions in Influencing Adherence Among HIV-Infected Individuals: A Systematic Review and Qualitative Meta-Synthesis. AIDS and Behavior. 2017;21(2):341-351.
29. Polit DF, Becks CT. Nursing Research: Generating and Assessing Evidence for Nursing Practice. 9th ed. Philadelphia: Wolters Kluwer / Lippincott Williams and Wilkins; 2012.
30. Bond W, Hussar DA. Detection of methods and strategies for improving medication compliance. American Journal of Public Health. 1991;48(9):1978-1988.
31. Nyanzi-Wakholi B, Lara AM, Munderi P, Gilks C. The charms and challenges of antiretroviral therapy in Uganda: the DART experience. AIDS Care. 2012;24: 137-142.

© 2021 Okuku and Dan-Jumbo; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

*Peer-review history:*  
*The peer review history for this paper can be accessed here:*  
<http://www.sdiarticle4.com/review-history/64746>