



## EVALUATION OF ADVERSE DRUG REACTION REPORTS IN ADULT PATIENTS ON ANTIRETROVIRAL THERAPY IN AHMADU BELLO UNIVERSITY TEACHING HOSPITAL ZARIA - NIGERIA

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### ABSTRACT

*Antiretroviral therapy (ART) has reduced morbidity and mortality in HIV patients. In Nigeria, there are over 400,000 patients on ART in over 200 secondary and tertiary hospitals. However, data on adverse drug reactions (ADRs) due to ARTs are limited. The aim of this study was to evaluate ADRs reports in adult patients on ART in Ahmadu Bello University Teaching Hospital Zaria (ABUTH). The study was a retrospective cross-sectional study on randomly selected adult patients on ART with ADR reports in Nasara Clinic of ABUTH, between January, 2012 and December, 2013. Medical records and ADR reports of the patients were reviewed and fitted into a structured questionnaire. Data were analyzed using SPSS Version 20.0. The study reviewed the records of 302 patients on ART as per the sample size out of a total of 1405 patients in the register within the study period. Of the 302 patients, 109 (36.1%) were reported to have at least one form of ADR, majority of whom were females 65 (59.6%). The most common ADRs were cough (34%), skin rash (44%), headache (20%) and diarrhea (10%), with few cases of anemia (5.5%), lipodystrophy (3.6%) and neuropathy (1.8%). 55% and 98% had concomitant disease and medications respectively. The actions taken to manage the ADR were; specific treatment of the ADR (69.7%), change of ARV regimen (22%) and few cases of hospitalization (6.4%). In conclusion, the study revealed the occurrence of ADRs in adult patients on ART in ABUTH. These reactions occurred within few months of medication, and were found to be related to age, social factor, ART regimen, gender, as well as other concomitant diseases and medications. Close monitoring is required to prevent severe ADR and improve adherence.*

**Keywords:** Antiretroviral therapy, adverse drug reaction, cough, retrospective

### INTRODUCTION

According to the world health organization, there were approximately 36.9 million people worldwide living with HIV/AIDS at the end of 2014. Sub Saharan Africa is the most affected region with 25.8 million people living with HIV in 2014 accounting for 70% of the global total of new HIV infection (Revell *et al.*, 2015). As of 2014 in Nigeria, the HIV prevalence rate among adults ages 15-49 was 3.17% making Nigeria the second-largest country with people living with HIV (CIA, 2014).

The treatment of HIV is known as antiretroviral therapy which is a combination of several antiretroviral drugs used to slow the rates which HIV replicates (WHO 2010). A combination of 3 or more antiretroviral drugs is more effective than using just one drug (monotherapy) to treat HIV. This is because combination therapy reduces the development of drug resistance and also gives a synergistic effect in suppressing viral replication (Bozic *et al.*, 2013).

The classes of antiretroviral drugs includes the following; Nucleoside reverse transcriptase inhibitors (NRTIs) e.g. Abacavir, Didanosine, Lamivudine, Stavudine, Zidovudine, Tenofovir; Non- Nucleoside reverse transcriptase inhibitors (NNRTs) e.g. Efavirenz, Nevirapine, Rilpivirin, Etarivine; Protease inhibitors (PI) e.g. Atazanavir, Lopinavir, Ritonavir; Fusion inhibitors (FI) e.g. Enfuvirtide; Integrase Inhibitor (II) e.g. Raltegravir; CCR5 receptor antagonist e.g. Maraviroc The drugs are formulated in a fixed dose combination consisting of two NRTIs and one NNRTI. And in some cases, fixed dose combination of two drugs from the same class.

The introduction of highly active antiretroviral therapy (HAART) in developed countries in the late 90s has been associated with a remarkable decrease in AIDS related mortality (CDC, 2005). These clinical benefits however are not without unwanted effects called ADRs. Just like every other drugs, ARVs have side effects and adverse drug reactions (ADRs).

Adverse drug reaction is a broad term referred to unwanted, uncomfortable or dangerous effect that a drug may have (Tarloff, 2012). In the United States 3-7% of all hospitalized patients are due to adverse drug reactions (Tarloff, 2012). Incidence of ADRs vary by patients' characteristics (e.g. Age, sex, ethnicity, co-existing disorders, genetic or geographic factors) and by drug factors (Tarloff, 2012). An adverse drug reaction is any noxious, undesired, or unintended response to a therapeutic agent/ which may be expected or unexpected, and may occur at dosages used for prophylaxis, diagnosis, or therapy of disease or for modifying physiologic function (WHO, 2010). Adverse drug reaction due to continuous exposure to antiretroviral drugs leaves the physician with few options; decreasing the dosage of ARVs thus compromising efficacy, withdrawing the offending drugs and substituting with another drug or symptomatically treating the ADR. However substituting the offending drug is difficult especially in resource limited settings, because most HAART regimens exists as fixed dose combinations (FDC) of different drugs most of which are first line drugs with high toxicity profiles (USAIDs, 2008). There are no known studies that provides reliable information on the ADRs in Northern

Nigeria. This indicates the need for antiretroviral therapy safety surveillance in clinical settings. This study is therefore aimed at evaluating ADRs in adult patients on ART in Ahmadu Bello University Teaching Hospital Zaria (ABUTH).

**METHODS**

The study was a retrospective cross-sectional study on 302 randomly selected adult patients on ART in ABUTH between the periods of January, 2012 and December, 2013 out of a total of 1405 patients registered within this period. Following ethical approval from ABUTH ethical committee, medical records and ADR reports of the patients were reviewed and fitted into a structured questionnaire. Only adult HIV positive patients on ART within the period of the study were included. The data collected were presented in tables as descriptive and percentages. They were analyzed using the SPSS Version 20.0.

**RESULTS**

**A. Baseline Characteristics of Study Population and Adverse Drug Reaction**

A total of 302 patients' medical records were reviewed. 109 out of the 302 patients developed ADR giving a prevalence 36.0%. Majority of the patients were females (58.6%) and mostly aged below 45 years (77.9%).

**Table 1: Baseline Characteristics of Study Population with Adverse Drug Reaction**

Variable	Category	Number of ADR (%)	
		Yes = 109 (36.1)	No = 193 (63.9)
Gender	Male	44 (40.4)	8 (42.0)
	Female	65 (59.6)	112 (58.0)
Age (Years)	18 - 25	14 (12.8)	36 (18.7)
	26 - 35	46 (42.2)	93 (48.2)
	36 - 45	25 (22.9)	46 (23.8)
	46 - 55	23 (21.1)	18 (9.3)
	56 Above	1 (0.9)	0 (0.0)

ADR = Adverse Drug Reaction

**A. Risk Factors Associated with Adverse Drug Reaction**

ADRs were more common in patients on TDF/3TC/EFV (38.5%). 38% of all pregnant women developed ADR. All patients smoking

(100%) and those taking alcohol (83.3%) had ADRs. 56% of patients with co-morbidity and those on concomitant medication especially septrin (68.8%) were reported to have ADR.

Table 2: Risk Factors Associated with ADRs

Variable	Category	Number of ADR (%)
ART Regimen	AZT/3TC/NVP	26 (23.9)
	TDF/3TC/EFV	42 (38.5)
	TDF/3TC	12 (11.0)
	AZT/3TC	29 (26.6)
Pregnancy	Yes	8 (38)
	No	13 (62)
Comorbidity	Yes	61 (56.0)
	No	48 (44.0)
Concomitant Medication	Septin	75 (68.8)
	Dapsone	8 (7.3)
	Multivitamins	17 (15.6)
	Anti-Tuberculosis	7 (6.4)
	None	2 (1.8)
Smoking	Yes	6 (100)
	No	0 (0)
Alcohol Consumption	Yes	20 (83.3)
	No	4 (16.7)

ART = Antiretroviral therapy; ADR = Adverse drug reaction; AZT = Zidovudine; 3TC = Lamivudine; NVP = Nevirapine; TDF = Tenofovir; EFV = Efavirenz; ADR = Adverse Drug Reaction

**B. Adverse Drug Reactions Encountered among the Study Population**

Patients totaling 109 (36.1%) on ART were found to have at least one form of ADR. The

mild form of the ADRs was mostly encountered (68.8%). They include and not limited to Rashes (15.9%) and Cough (12.6%). Specific treatments were mostly given to the patients (69.8%).

Table 3. ADRs encountered among the study population

Variable	Category	n (%); N = 109
Number of ADRs per patient	One	42 (38.5)
	Two	20 (18.3)
	Three	17 (15.6)
	Four	22 (20.2)
	Above Four	8 (7.3)
When ADR was experienced (Post medication)	< 2 Weeks	4 (3.7)
	2 Weeks - 1 Month	66 (60.6)
	1 Month - 3 Months	37 (33.9)
	> 3 Months	2 (1.8)
Severity of ADRs	Mild	75 (68.8)
	Moderate	27 (24.8)
	Severe	7 (6.4)
Interventions on ADR	Change of drug regimen	24 (22.0)
	Specific treatment	76 (69.8)
	Hospitalization	7 (6.4)
	None	2 (1.8)

**DISCUSSION**

This study reviewed adverse drug reaction (ADR) in adult patients taking antiretroviral medications. ADRs were not uncommon among the studied population. The occurrence of ADRs were to a larger extent associated with the antiretroviral therapy (ART) regimens, gender, comorbidity, concomitant medications and age. ADR was higher in patients below 45 years (77.9%). This is similar to previous findings by Eluwa *et al.*, (2012) who reported strong

correlation of HIV with adolescence. Our study showed more females with ADRs (59.6%) compared to their males counterpart (40.3%). This is similar to the report by Bonfati *et al.*, (2000) who observed that women experience significantly greater number of adverse effects. ADRs were found to occur within 1 month of initiating treatment (60.6%). 33.9% and 3.6% of the patients experienced ADRs in 1-3months and <2weeks of commencement of therapy respectively.

Similarly, Eluwa *et al.*, (2012) reported that the likelihood of ADR occurrence is highest in the first 6 months. Close monitoring of patients within this time frame is thus imperative to prevent the occurrence of severe ADRs and improves adherence. Eluwa *et al.*, (2012) also reported that 45% of reported ADRs occurred within 12-24 months of commencing ART. However, this was not observed in this study due to poor long term documentation at the Centre. Some studies have proposed time-dependent toxic accumulation as the mechanism of developing an ADR long after commencing medication.

Most of the reported ADR were mild (66.9%), 24.7% were moderate and 6.4% were severe. This suggests good tolerance level to ART in general. The commonest ADRs reported were cough, rash, itchy skin, headache, fever and diarrhea. Many of the cases of skin rash were reported in patients who received nevirapine-based regimen. The major clinical toxicity of nevirapine is rash which has been reported in 32% and 48% of patients (Tukukino *et al.*, 2008). National treatment guidelines recommend that a patient starting nevirapine should receive a 2-week lead-in dose (200mg once daily) to reduce the risk of rash and severity.

Incidence of anemia was 5% which occurred exclusively in patients on AZT/3TC/NVP. This is

similar to other studies carried out in Nigeria, Haiti and India that observed anemic rates of 3-12% (Subbaraman *et al.*, 2007 and Idoko *et al.*, 2002).

Studies on the incidence of ADR from developing countries have reported incidence of ADR between 11-35.9% (Patrice *et al.*, 2010; Bonfati *et al.*, 2000). According to Dean *et al.*, (2002), the incidence can occur as high as 54% in the presence of an opportunistic infection which is similar to this study where 55% of the patients had concomitant infection/disease/disorder.

Specific treatments were instituted in patients with ADR. The fact that ADR could be life threatening, serious attention is encouraged in ameliorating the ADR. This will improve on the overall treatment outcome and adherence.

## CONCLUSION

The study revealed the occurrence of Adverse Drug Reactions in adult patients on Anti-retroviral Therapy in Ahmadu Bello University Teaching Hospital Zaria. These reactions occurred within few months of medication, and were found to be associated with regimen, gender, as well as other concomitant medications. Close monitoring is required to prevent severe ADR and ART improve adherence.

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