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ORIGINAL

Prevalence of adverse drug effects of anti-retroviral drugs on HIV-positive patients receiving anti-retroviral treatment in General Hospital Onitsha, Anambra, Nigeria

Prevalencia de los efectos adversos de los medicamentos antirretrovirales en pacientes seropositivos que reciben tratamiento antirretroviral en el Hospital General de Onitsha, Anambra, Nigeria

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Abstract

Background: The wide use and acceptability of antiretroviral treatment has really helped in fighting HIV and keeping infected patients healthy and reducing the risk of further transmission and because of that HIV has become less life threatening. The general objective of this study was to determine the prevalence of adverse drug reactions of antiretroviral drugs on HIV patients receiving care in General Hospital Onitsha.

Methods: A descriptive cross sectional study was adopted to obtain findings on the Prevalence of Adverse Drug Reaction of Antiretroviral Drugs on HIV-positive patient in General Hospital Onitsha. A non-probability convenient sampling technique was used to determine a sample size of 310 respondents for the study and data was collected from all of them with the use of a detailed questionnaire. Data was analyzed using the SPSS version 22 and Microsoft excel. Chi-square was used to test association between variables.

Results: From the analysis, it showed that 65.8% of the respondents are female and adults in the age bracket of 29-48 years. 51.9% were married and majority of the respondents (80%) are of the Igbo origin. Also a good number of them (n=200, 64.5%) are using TDF+3TC+DTG. Only 37.1% of the respondents are found to have had an experience of adverse drug reactions in which skin rash, peripheral neuropathy and gastrointestinal problems are prevalent with percentages of 32.2, 23.5 and 22.6 respectively.

Conclusion: Adverse drug reactions associated with antiretroviral drugs in General Hospital Onitsha was found not to be prevalent and they occur mostly in people who are in the early years of treatment initiation. This study emphasized the need to monitor at risk and vulnerable patients to know when they have developed an event as a result of treatment. It is highly recommended that intensive and close follow-up of patients, especially for those in their early years of treatment initiation for early detection and quick management of adverse drug reaction.

Keywords: Adverse Drug Effects, HIV, Anti-retroviral Drugs, HIV-Positive Patients, Prevalence.

Resumen

Antecedentes. El amplio uso y la aceptación del tratamiento antirretroviral han ayudado realmente a luchar contra el VIH y a mantener sanos a los pacientes infectados y a reducir el riesgo de nuevas transmisiones, por lo que el VIH se ha convertido en una amenaza para la vida. El objetivo general de este estudio fue determinar la prevalencia de las reacciones adversas a los medicamentos antirretrovirales en los pacientes con VIH que reciben atención en el Hospital General de Onitsha.

Métodos. Se adoptó un estudio transversal descriptivo para obtener resultados sobre la Prevalencia de Reacciones Adversas a los Medicamentos Antirretrovirales en pacientes VIH positivos en el Hospital General de Onitsha. Se utilizó una técnica de muestreo conveniente no probabilístico para determinar un tamaño de muestra de 310 encuestados para el estudio y se recogieron datos de todos ellos con el uso de un cuestionario detallado. Los datos se analizaron con el SPSS versión 22 y Microsoft Excel. Se utilizó el chi-cuadrado para probar la asociación entre las variables.

Resultados. Del análisis se desprende que el 65,8% de los encuestados son mujeres y adultos en la franja de edad de 29 a 48 años. El 51,9% estaban casados y la mayoría de los encuestados (80%) son de origen igbo. Además, un buen número de ellos (n=200, 64,5%) utiliza TDF+3TC+DTG. Sólo el 37,1% de los encuestados ha experimentado reacciones adversas al fármaco, en las que prevalecen las erupciones cutáneas, la neuropatía periférica y los problemas gastrointestinales, con porcentajes de 32,2, 23,5 y 22,6 respectivamente.

Conclusión. Se encontró que las reacciones adversas a los medicamentos antirretrovirales en el Hospital General de Onitsha no son prevalentes y ocurren principalmente en las personas que están en los primeros años de la iniciación del tratamiento. Este estudio enfatiza la necesidad de monitorizar a los pacientes de riesgo y vulnerables para saber cuándo han desarrollado un evento como resultado del tratamiento. Se recomienda encarecidamente realizar un seguimiento intensivo y estrecho de los pacientes, especialmente de los que se encuentran en los primeros años de inicio del tratamiento, para la detección precoz y el manejo rápido de las reacciones adversas a los medicamentos.

Palabras clave: Efectos adversos de los medicamentos, VIH, medicamentos antirretrovirales, pacientes seropositivos, prevalencia.

Introduction

Anti-retroviral treatment is the most effective tool in helping fight the Human Immunodeficiency Virus (HIV) by keeping infected patients healthy and reducing the risk of further transmission. As countries implement the 2017 World Health Organization (WHO) treatment guidelines, which require all people living with HIV to be on long-term treatment[1], It is proven that effective treatment results in a decrease in viral load, a boost in the number of CD4 counts, and clinical improvement of the HIV-infected patient[2]. Therefore, ARV drugs have brought highly significant hope to people living with HIV as millions of eligible HIV-infected patients have access to life-prolonging ARV drugs, which has led to a reasonable decrease in HIV-related morbidity and mortality[3]. As a result, HIV has gone from a life-threatening to a chronic condition as a result of the wide use and accessibility of anti-retroviral treatment (ART) among HIV patients[4]. It is estimated that out of the 35.3 million people living with HIV worldwide, only 10.6 million were receiving ART in 2012, with nearly 6.6 million HIV/AIDS related deaths worldwide having been prevented using ART[5]. According to[6], the sub-Saharan African region is most affected by HIV; more than 67% of the people were infected with HIV, and 72% of the patients have died since 2008 due to Acquired Immune Deficiency Syndrome (AIDS)[7]. At the same time[6], reports indicated that approximately 36.7 million people were living with HIV/AIDS, with only 18.2 million receiving anti-retroviral treatment globally.

In 2004, Nigeria received over 400 million dollars in funding to scale up ART –a funding that was partly implemented by Family Health International under the Global HIV/AIDS Initiative Nigeria (GHAIN) project– and this resulted in the influx of ART into the country at an increased level[3]. The establishment of eligibility is attained using clinical staging and CD4 count (Stage I or II with a CD4 count less than 350 or stage IV irrespective of CD4 counts for adults; CD4 less than 25% for children less than 11 months and CD4 less than 20% for children between the ages of 12-35 months) as a criteria regarding Nigerian national guidelines[8].

Despite these gains, adverse reactions to these medicines remain a highly significant public health concern, which stands to contradict the effectiveness of anti-retroviral treatment[2]. Adverse drug reactions are a critical component of HIV/AIDS care and treatment as they should be evaluated for the prevalence and pathogenesis of ADRs to inform clinical management[9]. The occurrence of ADRs may negatively affect the quality of life of patients as well as adherence to the treatment, and the spectrum of ADRs is wide and varied, making it difficult to identify the principal cause[10]. ADRs are highly significant in the effort to diminish toxicities that are most likely to increase the prevalence of chronic diseases of ageing in the HIV-positive population[4]. A better understanding of the ADRs of ARV drugs among HIV patients could help specialists to optimize therapy and also improve the care given to HIV-positive patients[9].

Adverse drug reactions are the most common reason for poor adherence to ART[3]. Non-adherence to anti-retroviral treatment regimens remains common, leading to considerable deterioration of the disease and enhanced HC expenditure[11]. Noncompliance is also thought to increase viral load, drug resistance, and treatment failure[12]. Chronic use of ARV drugs, multiple pills taken at once, exclusion from society and being lonely due to stigma and discrimination, and treatment failure are the major problems associated with highly active anti-retroviral treatment[13]. Adverse drug reactions (ADRs) are regarded as the most prevailing cause of mortality among people living with HIV/AIDS as they are significantly involved in treatment interruptions, regimen changes, treatment failure, and non-adherence among patients on ART[13]. ADRs are brought about by many factors, including stock-out of drugs, poor health service quality, and treatment interruptions, which limit the treatment options, increase the cost of treatment programs, and might increase resistant viruses to the point of being transmissible if left untreated[14]. ADRs are not exactly life-threatening but can impact negatively on the quality of life as it impairs the patients' willingness to adhere to their regimen and influences the decisions made about health care[15].

The stock out of drugs interrupts the treatment and may contribute to ARV drug resistance. That could urge regimen change to deter ARV drug resistance. The longer a patient is on ART, the less likely they will experience ADRs, possibly as a result of stability in the ARV regimen, coming after many changes and eventually settling on an acceptable regimen[16]. Previous research has shown that patients over the age of 38 years have a significantly higher recurrence of ADRs than those under the age of 30 years[17,3]. Also, gender differentials were also found with females having higher risks of adverse drug effects than males, as females experienced higher abnormal fat distribution and peripheral neuropathy that occurred at a significantly younger age compared to males[16]. In a multisite trial in Africa, it was found that tenofovir therapy was associated with a 1.3% rate of significant nephrotoxicity, which was comparable to other regimens, thereby showing no significant toxicity difference between tenofovir and other regimens[3]. This raises a sentinel sign that perhaps drug response to TDF in this setting is not in conformity with the results from other studies where the drug profile of TDF has been superior over AZT and d4T.

The problematic occurrence of widespread underreporting of ADRs and the importance of addressing shortcomings effectively in pharmacovigilance activities in the public healthcare setting need to be appropriately addressed[18]. Furthermore, knowledge regarding antiretroviral (ARV) toxicity in developing countries is limited. These toxicities

can result in unknown long-term effects and compromise patient confidence and adherence[19]. Poor adherence, particularly at levels lower than 95%, has a negative impact on HIV outcome[20]. Over the years, some adverse drug reactions have been observed in every course of anti-retroviral therapy[7]. The occurrence of adverse drug reactions negatively affects the quality of life of patients as well as adherence to the treatment, and the spectrum of adverse events is wide and varied, thereby making it difficult to identify the principal cause sometimes[10]. Different types of anti-retroviral adverse drug reactions occur commonly among patients. Because the ADRs vary in their severity, a common cause of ADR is therefore poor adherence. Also, monitoring safety and toxicity related to ART remains a challenge facing the public health sector. Spontaneous reporting of ADRs is a very inefficient system for detecting drug-related conditions, leading to an underestimation of the burden due to adverse drug reactions. Structured surveillance tracks HIV positive patients who are on ART to assess drug-related morbidity and mortality over time. The objective of this study was to determine the prevalence of adverse drug effects of anti-retroviral drugs on HIV-positive patients who are receiving anti-retroviral treatment in General Hospital Onitsha.

Methods

Design

A descriptive cross-sectional design was adopted in the study on the prevalence of adverse drug effects of anti-retroviral drugs on HIV-positive patients who are receiving anti-retroviral treatment in General Hospital Onitsha.

Study Setting

This study was carried out at General Hospital Onitsha, Onitsha South Local Government Area, Anambra State. General Hospital Onitsha is a government-owned tertiary healthcare facility located in the cosmopolitan city of Onitsha in the southeastern zone of Nigeria. It has several departments, just like every other government hospital. Services at the ART unit are provided by a group of competent health and non-health professionals. The unit provides comprehensive HIV-related services such as voluntary counselling and testing (VCT), provider-initiated testing and counselling (PITC), PMTCT, pediatric HIV care, and treatment and support for PLWHAs.

Inclusion Criteria

The study recruited HIV-positive patients less than 18 years who were receiving anti-retroviral treatment in General Hospital Onitsha, at least for a minimum of 6 months.

Exclusion Criteria

The study excluded HIV-positive patients receiving treatment in General Hospital Onitsha who refused to give in their consent for the study. The study also excluded HIV-positive patients who are absent at the time of study, those who are below the age of 18, and those who picked up ARVs only once at the pharmacy.

Sampling

The researcher made use of only three hundred and ten HIV-infected patients receiving anti-retroviral care in General Hospital Onitsha. The respondents will be interviewed in order to gather information for the progress of the study.

Sample Size determination

The sample size was determined using the Yamene formula (1967) for sample size determination.

$$n = \frac{N}{1+Ne^2}$$

Where;
n is the desired sample size
N is the population size (953)
e is margin of error (0.05)

$$n = \frac{953}{1+953(0.05)^2}$$

$$n = \frac{953}{1+953*0.0025}$$

Therefore,
n = 281.74

Furthermore, to account for Non Response Rate, the sample size was increased by 10% = 0.10 = 281.74 x 0.10 = 28.1

n =281.7+28.17 =309.9
Approximately =310

Sampling Techniques

A non-probability-based convenience sampling technique was employed for the study on the prevalence of adverse drug effects of anti-retroviral drugs on HIV-1 and HIV-2 patients who are receiving anti-retroviral treatment in General Hospital Onitsha.

Data Collection

A self-administered structured questionnaire was used for the study on the prevalence of adverse drug effects of anti-retroviral drugs on HIV-positive patients who are receiving anti-retroviral treatment in General Hospital Onitsha. Data was obtained using a self-administered, semi-structured questionnaire. This was done with the aid of two (2) field assistants who work in the ART department unit of the hospital to aid the researcher in the data collection process. Both the researcher and the research assistants were involved in retrieving the administered questionnaire for data analysis.

Validity and Reliability of the Research Instrument

The questionnaire as the instrument of data collection was developed by the researcher and submitted to the project supervisor for face validity and proper scrutiny as well as two other lecturers in order to ensure that the questionnaire meets the objectives of study before the distribution of questionnaires for reliability testing.

The reliability of the data instrument was determined using the test retest method. The researcher gave copies of the questionnaire to some respondents outside the area of study by the researcher, thereby pre-testing the questionnaire twice before administering it to the respondents. This area shares similar characteristics with General Hospital Onitsha, which was used for this study. On reliability correlation testing using SPSS, the Cronbach alpha value of 0.76 was obtained. The closeness of this value to 1 indicates that the instrument of data collection is very reliable.

Method of Data Analysis

The data that was gathered from the questionnaire was analyzed using the statistical package for social sciences (SPSS) version 22 and Microsoft Excel. Descriptive statistics, which were expressed in frequency tables and percentages, were used to describe the characteristics in the study of the subjects. Inferential statistics were used with a confidence interval of 95% and a P-value of 0.05 for interpreting significance and correlation.

Ethics

A letter of introduction was obtained from the ethics committee, department of public health, Federal University of Technology Owerri (FUTO). The letter was handed over to the Head of Department, Anti-retroviral Therapy (ART) unit, General Hospital Onitsha, in order to get his consent before carrying out the research in the unit. The purpose of the research was explained to each respondent and verbally informed consent was obtained from them before inclusion in the study. Also, the anonymity of the respondents was assured and ensured. The confidentiality of the information they gave had to be maintained.

Results

A total of 310 respondents were included in the final analysis. 310 questionnaires were carefully distributed and collected by the researcher for the study. The questionnaires were filled properly and cross-checked for accuracy. The flow diagram below (**Figure 1**) summarizes the distribution of patients according to their antiretroviral treatment regimen. This study final analysis includes only HIV-positive patients above the age of 18 who are receiving antiretroviral treatment in General Hospital Onitsha.

The flow diagram (**Figure 1**) summarizes the distribution of respondents according to their antiretroviral treatment regimen. As shown in the figure above, 66.5% (n=206) of the total population use combination of two nucleoside reverse transcriptase inhibitors (NRTI) and an integrase inhibitor (II); 29.6% (n=92) use combination of two NRTI and a non-nucleoside reverse transcriptase inhibitor (NNRTI); and the remaining 3.9% (n=12) use the combination of two NRTI and a protease inhibitor (PI).

Figure 1: Flow diagram of patients and ART regimen received at treatment initiation.

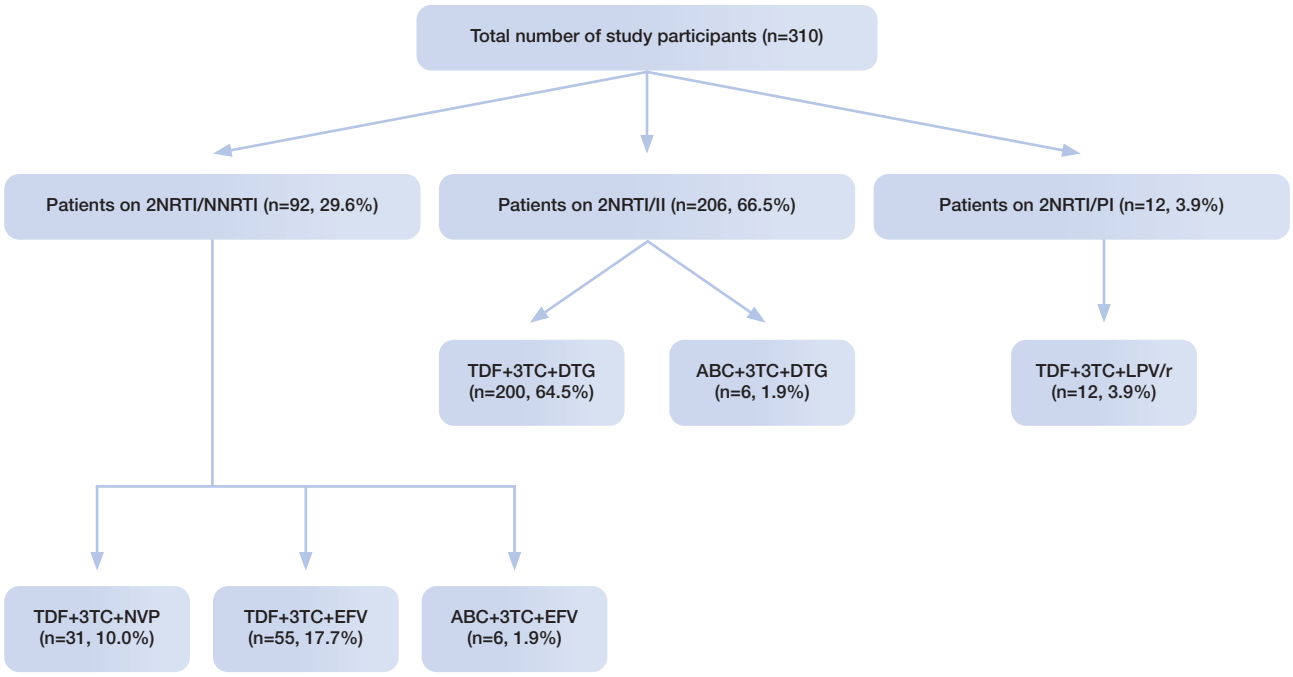

Table I: Socio-demographic Characteristics of Study Participants. (N=310).

Variables	Subgroup	Frequency (N=310)	Percentage (100%)
Age	18-28	59	19.0
	29-38	71	22.9
	39-48	115	37.1
	49-58	35	11.3
	58 and above	30	9.7
Gender	Male	106	34.2
	Female	204	65.8
Marital status	Single	66	21.3
	Married	161	51.9
	Divorced/Separated	31	10.0
	Widowed	52	16.8
Ethnicity	Igbo	248	80
	Hausa	37	11.9
	Yoruba	17	5.5
	Others	8	2.6
Educational level	Primary	44	14.2
	Secondary	75	24.2
	Tertiary	104	33.5
	Uneducated	87	28.1
Occupation	Trader	137	44.2
	Farmer	95	30.6
	Civil servant	33	10.6
	Student	21	6.8
	Others	7	2.3
	Unemployed	17	5.5

Source: Field data, 2021.

Table I above shows that a good number of the study participants were females (n=204, 65.8%) and adults in the age bracket of 39-48 years. Many of the participants (n=104, 33.5%) have attained tertiary education, 87(28.1%) are uneducated, 75(24.2%) are recorded to have achieved only secondary education and 44(14.2%) attained only primary education. Regarding marital status, married people are highest accounting for 51.9% of the total population, seconded by the singles (n=66, 21.3%), then the widowed (n=52, 16.8%) and the divorced/separated (n=31, 10%). Considering ethnicity, Igbos are leading amounting to 80% of the population, followed by the Hausas (11.9%), then the Yorubas (5.5%) and then few people from other tribes(2.6%). It is also shown in the table above that most of the study participants are traders with a percentage of 44.2, seconded by farmers with a percentage of 30.6, then comes civil servants, students, people of other occupations not mentioned and unemployed people with a percentage of 10.6, 6.8, 2.3, and 5.5 respectively.

Figure 2: A bar chart representing the age distribution of respondents.

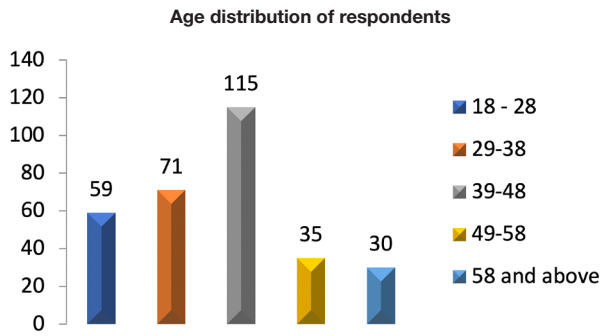

Figure 2 shows a diagrammatic representation of the age distribution of the respondents plotted against the frequency of respondents found to be within these age groups. As shown in the diagram, the leading age group is those within the ages of 39-48 years (n=115), while the least one is found to be those who are 58 years and above (n=30).

Table II: Ascertaining Type, Frequency and Dosage of ARV in Use.

Characteristics	Sub-group	Frequency (n=310)	Percent (100%)
How long the patient has been on treatment	6 months-2 years	139	44.8
	2-6 years	57	18.4
	7-10 years	98	31.6
	Above 10 years	16	5.2
The ARV combination in use	2NRTI/II	206	66.5
	2NRTI/NNRTI	92	29.6
	2NRTI/PI	12	3.9
The exact drug combination in use	TDF+3TC+DTG	200	64.5
	TDF+3TC+EFV	55	17.7
	TDF+3TC+LPV/r	12	3.9
	ABC+3TC+EFV	6	1.9
	TDF+3TC+NVP	31	10.0
	ABC+3TC+DTG	6	1.9
Prescribed dosage of the drug	1 tab/daily	288	92.9
	2 tabs/daily	22	7.1
Adherence to everyday use of drug	Yes	199	64.2
	No	35	11.3
	Sometimes	76	24.5
Adherence of everyday use of drug with respect to time and dosage	Yes	178	57.4
	No	46	14.8
	Sometimes	86	27.7

Source: Field data, 2021.

Table II indicates that 139(44.8%) to have been on treatment for the first 2 years, 57 are reported to fall within those receiving treatment for the past 2-6 years, 98 have been on treatment for about 7-10 years and the rest (n=16,5.2%) have been on treatment for over 10 years. It also shows that all that study participants make use of ARV drugs of which the common ones are TDF+3TC+DTG (66.5%), TDF+3TC+EFV (17.7%) and TDF+3TC+NVP (10.0%) while the least common ones areTDF+3TC+LPV/r (3.9%) and ABC+3TC+EFV and ABC+3TC+DTG with percentages of 1.9% each. Almost all the respondents (92.9%) report their prescription to be 1tab/day and the rest (7.1%) take theirs twice daily. 64.2% of the study participants adhere to everyday use of drug, 11.3% do not adhere while 24.5% adhere sometimes. 57.4% of the total population adhere to everyday use with respect to time and dosage, 14.8% do not and the remaining 27.7% sometimes adhere to everyday use of drugs with respect to time and dosage.

Figure 3 is a pie chart representing the how long respondents have been on treatment, hence the time treatment initiation. From the chart, it is seen that 44.8% of the total population are within the first three years of treatment, 18.4% reported to have been on treatment for about 3-6 years, 31.6% have been on treatment for about 7-10 years, and the remaining 5.2% have been on antiretroviral treatment for more than 10 years.

Figure 3: A pie chart representing how long a patient has been on treatment.

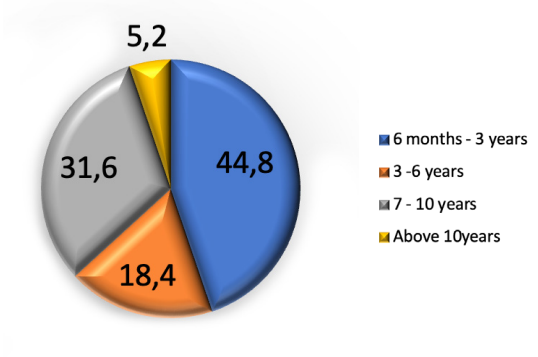

Table III: Ascertaining the incidence of ADRs resulting from ARV drugs.

Variables	Sub-groups	Frequency	Percent
Ever experienced any ADR	Yes No	115 195	37.1 62.9
What type of ADR experienced	Neuropathy Skin rash/itching Insomnia Dizziness Gastro-intestinal	27 37 10 15 26	23.5 32.2 8.7 13.0 22.6
Presence of severe condition as a result of ADR	Yes No	26 89	22.6 77.4

Source: Field data, 2021.

Table III shows that only 37.1% (n=115) adverse drug reaction of antiretroviral drugs of which 22.6% experience severe conditions as a result and 77.4% never had such experience. The adverse events experienced by the respondents include skin rash/itching, neuropathy, insomnia, dizziness and gastro-intestinal symptoms with percentages of 32.2, 23.5, 22.6, 13.0 and 8.7 respectively.

Figure 4: A bar chart showing percentage distribution of ADR types.

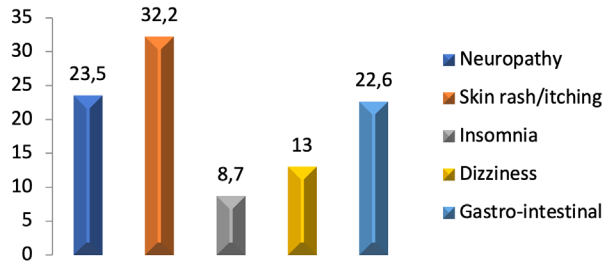

Table IV: Determining rate of occurrence and result on switching.

Variables	Sub-groups	Frequency	Percent
Rate of occurrence	Weekly Monthly Yearly Rarely	0 21 40 54	0 18.3 34.8 46.9
Ever had a change in regimen	Yes No	73 42	63.5 36.5
Result of ADRs after drug switching	Disappeared Reduced/contained	29 44	39.7 60.3

Source: Field data, 2021.

Table IV shows that of 115 patients that experience adverse events, 21(18.3%) have them occur every month, 40(34.8%) experience it yearly and 54(46.9%) rarely have the experience. 63.5% of those that experience adverse events have had a change in regimen, of which 39.7% had the adverse events disappear after switching and 60.3% had their adverse events reduced or contained.

Figure 4 is another bar chart representing the percentage distribution of the types of adverse drug reactions (ADRs) experienced by the respondents. As shown above, the

Table V: Association of participants' demographic factors and adherence to prescribed dosage and frequency of drug use.

Variables	Sub-group	Patients with ADR	Patients without ADR	Chi-square test value	Df	P value	Decision
Age	18 - 28 29 - 38 39 - 48 49 - 58 59 and above	3 20 48 14 30	36 51 67 21 0	80.393	4	.0001	Sig
Gender	Male Female	55 60	51 144	15.100	1	.0001	Sig
Educational Level	Primary Secondary Tertiary Uneducated	24 20 28 43	20 55 76 44	19.517	3	.0001	Sig
Marital Status	Single Married Divorced Windowed	28 58 9 20	38 103 22 32	1.788	3	.618	Not Sig.
How long patient has been on treatment	6 mths - 3 yrs 3 - 6 years 7 - 10 years Above 10 yrs	75 27 12 1	64 30 86 15	51.972	3	.0001	Sig
Adherence to with respect to dosage and time	Yes No Sometimes	36 29 50	142 17 36	51.305	2	.0001	Sig

Source: Field data, 2021.

most prevalent ADRs are skin rash, neuropathy and nausea/vomiting with percentages of 32.2, 23.5 and 22.6 respectively. The least occurring ones are dizziness and insomnia with percentages of 13.0 and 8.7 respectively.

Test of Hypothesis

Table V shows that age, gender, educational level, the time of treatment initiation and the patients' adherence to everyday use of drugs with respect to prescribed dosage and time all appear to have a correlation with the patients' experience of adverse effect with p value of 0.0001 each. Marital status is not significant in determining the experience of adverse drug reaction of antiretroviral drugs.

Discussion

From the analysis, it is revealed that the majority of the respondents (80%)of the study are of Igbo origin. This is because the study was conducted in the Southern part of Nigeria as the hospital is located in Onitsha, Anambra State. Considering the socio-demographic characteristics of the respondents, with regards to gender and age, a good number of respondents (65.8%) are females, and most respondents are within the age range of 29-48 years old. This is in accordance with the findings of[21], that the majority of these patients are females and young adults in the age bracket of 25-45 years old. This gender difference, though not statistically significant, is found in much other related research carried out in African countries. It is also consistent with other studies conducted in Nigeria that show a feminization of the HIV epidemic[22,23,21]. Findings from the study show that 44.8% of the respondents are within their first three years of treatment, 18.4% reported to have been on treatment for about 3-6 years, 31.6% have been on treatment for about 7-10 years, and the remaining 5.2% have been on antiretroviral treatment for more than 10 years. A good percentage of the respondents (66.5%) use a combination of two nucleoside reverse transcriptase inhibitors (NRTI) and an integrase inhibitor (II). Following suit is the group using the 2NRTI/NNRTI combination. People who make use of the ABC+3TC+EFV and ABC+3TC+DTG are 6 and 6, respectively, which is a minority representative of the study participants. This is because the patients who use these drugs are ones with special cases, for instance, patients with kidney and liver diseases and children (which we didn't use for this study).

Almost all the respondents (n = 200, 64.5%) make use of TDF + 3TC + DTG. This is because it is the first line regimen and it is suitable for virtually every adult, including pregnant and lactating mothers, and also for adolescents. Meanwhile, TDF + 3TC + LPV is taken by a small number of people (n = 12,3.9%) because it is a second-line regimen.

Considering the frequency and dosage, it is denoted here that the majority of the study participants (n=199,64.2%) adhere to everyday use of their drugs, of which 89.4% adhere to everyday use of the drugs with respect to the time and required dosage. 11% of the study participants do not adhere at all, and 24.5% do not adhere all the time as their answers to questions are sometimes. This argues the study conducted by[24] that says this presents less than optimal adherence among HIV-positive patients. Almost all respondents (n=288,92.9%) are taking one tablet per day, while the remainder (n=22,7.1%) are taking two tablets per day because they are on second-line therapy TDF + 3TC+LPV and abacavir-based regimens. From the findings, 115 participants out of the 310 used for the study were reported to have experienced or be experiencing adverse drug reactions as a result of the use of ARV drugs[23]. This represents 37.1 % of the total population and is in accordance with[23]. Of the people that have experienced ADRs, 26(22.6%) have experienced a chronic condition as a result of the ADRs, while 89 (77.6%) haven't had such experience. The prevalent ADRs are skin rash/itching, neuropathy and gastro-intestinal symptoms (which include vomiting, nausea, abdominal pain and diarrhea) with percentages of 32.2%, 23.5% and 22.6%, respectively, which is the same as reported by other Nigerian studies[3,22,21]. In comparison to[23], the study found a lower incidence of antiretroviral drug adverse drug reactions. Adverse events are reported to be most prevalent among people who are in the early years of treatment initiation, and this supports the study[3] that found ADRs are more likely to occur within the first 6 months of treatment. The study shows that the 54 respondents(46.9%) out of 115 that were reported to have had an experience of ADR rarely have the occurrence, 40(34.8%) experience it yearly and 21(18.3%) experience it monthly. Also, 63.5% of those reported to be with ADR have had a change in regimen, of which 39.7% (n=29) reported that the ADR had disappeared and 60.3% (n=44) reported ADRs to be reduced or contained. This is because most respondents are still adjusting to the treatment while few are allergic to a combination of the regimen.

Conclusion

Adverse drug reactions to antiretroviral treatment were common in this study and were reported to occur mostly within the early years of treatment initiation. The most prevalent ADRs were skin rash/itching (n=37, 32.2%), neuropathy (n=27, 23.5%) and gastro-intestinal symptoms (n=26, 22.6%). Other rarely occurring but serious cases of ADR include insomnia (n=10,8.7%) and dizziness (n=15,13%), which were also observed. Adverse Drug Reactions are significantly predicted by the time of therapy initiation as people within the early years of initiation were reported to experience ADRs more than others, with a percentage of 65.2%. This study

emphasizes the need to monitor at-risk and vulnerable or low-immune patients to know when they have developed an event as a result of treatment.

Recommendations

As a result of this study, an intensive and close follow-up of patients, especially in the early years of treatment initiation, is highly recommended for early detection of ADR and quick management. These ADRs should be properly documented in order to provide accurate data for further studies or research. Patients who are not able to respond effectively to first-line therapies should be identified and placed on effective second-line therapies. Valuable information on patients' responsiveness to treatment should be made available to physicians in-charge and concerned NGOs like USAID when there is a need to modify HAART regimens. Further study using larger and more complete data is also recommended.

Limitations of the Study

With regards to the study, there is a tendency that non-clinical ADRs were overlooked. There is a possibility of under-reporting of ADRs by patients and caregivers. The researcher was not able to relate the factors that caused the ADRs, which would have played an important role in the interpretation of the result.

Ethics Approval and consent to Participate

Not Applicable.

Consent to Publish

Not applicable.

Availability of Data and Materials

The Data set from the study are available to the corresponding author upon request.

Competing Interests

Authors have declared that they have no competing interests.

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Questionnaire on adverse drug effects of anti-retroviral drugs on HIV-positive patients who are receiving anti-retroviral treatment in General Gospital Onitsha, Anambra

SECTION A

This section covers for the Demographic Data

1. Gender

Male ☐ Female ☐

2. Educational qualifications

Primary
Secondary
Tertiary
No formal education

3. How old are you?

18-2829-3839-4849-5859 and above

4. What ethnic group do you belong to?

Igbo ☐ Hausa ☐ Yoruba ☐ Others ☐

5. What is your occupation

Trader Farmer Civil servant Student
Others

6. Marital status

Single ☐ Married ☐ Divorced ☐ Widowed ☐

SECTION B

This section is to ascertain frequency of use and dosage of ARV drugs

7. How long have you been on antiretroviral therapy?

6 months-2 years ☐
2-6 years ☐
7-10 years ☐
Above 10 years ☐

8. Which of the ARV drug combination are you on?

2NRTI/NNTRI ☐ 2NRTI/ PI 2NRTI/II ☐

9. What is the specific regimen in use?

TDF+3TC+DTG ☐
TDF+3TC+EFV ☐
TDF+3TC+LPV/r ☐
ABC+3TC+EFV ☐
TDF+3TC+NVP ☐
ABC+3TC+DTG ☐

10. What is the prescribe dosage of the drug

1tab/day ☐ 2tabs/day ☐

11. Do you adhere to everyday use of drugs

Yes ☐ No ☐ Sometimes ☐

12. Do you adhere to drugs use with respect to prescribed time and dosage

Yes ☐ No ☐ Sometimes ☐

SECTION C

To ascertain the adverse drug reaction experienced

13. Have you ever noticed any change in your body since the use of the drug

Yes ☐ No ☐

14. If yes, what kind of changes

Neuropathy ☐
Skin rash/itching ☐
Insomnia ☐
Dizziness ☐
Gastrointestinal issues ☐
If others, Indicate .....

15. Do you have any chronic condition as a result of the dug intake

Yes ☐ No ☐

SECTION D

To determine the rate of ADRs

16. How often do you notice these change

Weekly ☐ Monthly ☐ Yearly ☐ Rarely ☐

17. Have you ever had any change in regimen

Yes ☐ No ☐

18. What is the result of ADRs after switching

Disappeared ☐ Contained /Reduced ☐

Thanks for your maximum co-operation, your confidentiality is guaranteed

APPENDIX 3
Research workplan

S/N	ACTIVITY	TIME FRAME	PERSONNEL RESPONSIBLE
1	Development and submission of research proposal	8 weeks	Researcher
2	Project proposal	1 day	Researcher
3	Recruitment and training of research assistants	1 week	Researcher
4	Pre-testing of instrument of data collection (questionnaire)	1 week	Researcher
5	Analysis of pre-tested questionnaire	5 days	Researcher
6	Modification of data collection tool	2 days	Researcher
7	Data collection	4 weeks	Researcher and research assistants
8	Analysis of data and report conclusion	6 weeks	Researcher
	Total time spent for the study	**21 weeks and 1 day**	

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