

# Assessment of Pharmacotherapy of People Living with HIV/AIDS Attending Antiretroviral Therapy Clinic in a Tertiary Hospital in Ilorin.

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## Abstract

The evaluation of Pharmacotherapy in People Living With Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) (PLWHA) is crucial since it will direct and facilitate good patient care. To evaluate the different medications used by HIV/AIDS patients attending the University of Ilorin Teaching Hospital, Ilorin, antiretroviral adequacy (ART) clinic.

The clinical data of HIV/AIDS patients receiving therapy at the ART clinic at University of Ilorin Teaching Hospital (UIH), Kwara State, Nigeria, were retrospectively reviewed and evaluated between July 2022 and December 2022 using a validated data capture form designed for the study.

A total of 1615 case files were retrieved between the period of study. Four hundred case files that met the inclusion criteria were reviewed and included in the study. The modal age group was 31–40 years (n=120, 30%) and gender distribution showed female preponderance (n=259, 64.7%). The general physical examination documented was grossly inadequate, as it was only reported in one-third of the patients. Only a quarter of the patient had the documentation of the use of non-HIV drugs and the most frequently prescribed one was co-trimoxazole while the most prescribed antiretroviral drug was the combination of tenofovir, lamivudine and dolutegravir. A number of PLWHA attending the ART clinic did not have a comprehensive physical examination done. This may hinder the diagnosis of other medical conditions that might be present and requires treatment. The laboratory work-up was inadequate and may affect treatment outcomes. The documentation of the use of non-HIV medications was grossly inadequate, this may potentiate drug-drug interactions and adverse drug reactions.

**Key words:** Medication, Antiretroviral, Human Immunodeficiency Virus, Hospital.

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## Introduction

Health, the development of human capital, and the economy have all been significantly impacted by the Human Immunodeficiency Virus (HIV).<sup>1</sup> The illness undermines social and economic development due to its impact on the well-being of families, longevity, and economic growth. Human immune deficiency virus infection and the emergence of AIDS have posed a serious threat to human health on a global scale. It is still a major public health concern in many countries, notably those in sub-Saharan Africa.<sup>2</sup>

In 2021, the UNAIDS program estimated that there were 37.7 million people worldwide living with HIV and that 680,000 people had died from the infection.<sup>3</sup> One of the most significant advancements in the fight against the HIV pandemic was Highly Active Antiretroviral Therapy (HAART). The general health and quality of life of persons with HIV/AIDS have improved dramatically as a result of the use of HAART.<sup>4</sup> Also, it has greatly reduced HIV-related morbidity and mortality.<sup>4</sup>

With HAART, three or more ARV medications—each with a different mechanism of action—from at least two different classes—are given simultaneously to halt HIV replication. It serves as the accepted standard of care for people with HIV.<sup>5</sup> This strategy was developed in response to the knowledge that treating HIV infection with just one or two ARV drugs could result in rapid treatment failure and the development of drug resistance, which could restrict the efficacy of any potential therapeutic alternatives in the future.<sup>6</sup> The most crucial intervention in terms of enhancing patients' functional and clinical status and preventing opportunistic infections that aggravate the illness and impair the prognosis is effective antiretroviral medication.<sup>7-8</sup>

Since the advent of highly active antiretroviral medication 25 years ago, the HIV infection has been transformed from an infection that is essentially incurable to a chronic, manageable disease.<sup>9-12</sup> Like the general population, PLWHA are susceptible to other illnesses that can necessitate the use of non-HIV drugs.<sup>13</sup> Certain non-HIV medications could interact with HAART and have mild to severe negative effects, which could result in poor medication adherence, drug-drug interactions, adverse drug reactions, treatment termination, and a change in antiretroviral drug

combinations.<sup>14</sup>

Depending on their clinical condition and test results, patients are given a variety of HAART combinations. There are limited studies that evaluates the use of HAART concurrently with non-HIV medications especially in sub-Saharan African nations including Nigeria.<sup>15</sup>

Consequently, the objective of this study was to assess the HAART medications co-prescribed with non-HIV medications and the various antiretroviral drug combinations in use by PLWHA who attended the ART clinic.

### Material and Methods

This study was carried out at the Antiretroviral therapy clinic of University of Ilorin Teaching Hospital, Ilorin. UITH is a 600-bed facility that is located in Ilorin, the capital of Kwara state in the North Central geopolitical zone of Nigeria. UITH is a federal tertiary hospital that treats patients from both within and outside the state and acts as a referral hub.

We retrospectively reviewed and analyzed the clinical records of PLWHA who were receiving treatment at the ART clinic in UITH between July 2022 and December 2022 using a validated data capture form. The ART clinic opens from 8 am to 4 pm, Monday through Friday. About 200 new and old patients (adults and children) treated each day. A little over 6,000 registered patients with HIV are given free antiretroviral medications each month for HIV/AIDS including men, pregnant and non-pregnant women and children from different parts of the state and Nigeria.

The researchers used the main register they obtained from the ART clinic medical record section to find eligible cases. Using a web-based random sampling technique, a unique identification number was given to each case file after it was randomly chosen. Using the validated data capture form, one of the researchers went through the case files. Information on the sociodemographic characteristics, clinical history, physical examination findings, the HAART combination prescribed and other co-prescribed drugs were extracted. Other important information extracted included the results of routine CD4 Count, Viral load, hematological investigations, electrolyte, urea and creatinine at baseline and follow-up. Two other researchers verified the data that had initially been extracted. Using Kappa statistics, there was 90% agreement among the three reviewers. A fourth reviewer's (Clinical Pharmacologist) viewpoint surpassed in areas where there were discrepancies. The Sample Size was determined by using the Fisher's formula<sup>16</sup> and a source prevalence from previous studies<sup>17</sup>, giving a minimum sample size of 384. Ethical approval was obtained from the Ethics and Research Committee of the UITH with approval number **ERC PAN/2022/04/0251**. Strict confidentiality was

maintained about the particulars of the patients during and after the study.

Male and Female patients 18 years of age with confirmed HIV infection on treatment with HAART for at least one month. Patients who died during the course of treatment, stopped or changed treatment were also included in the study.

Children and pregnant women with confirmed HIV infection were excluded from the study. Patients that have been confirmed with the HIV infection but are yet to commence HAART were also excluded.

The data were analyzed using IBM SPSS statistics software, version 22. With the aid of descriptive statistics, the demographic and clinical characteristics were compiled. For categorical data, frequencies and percentages were utilized. The significance level was determined at  $p < 0.05$ . Prior to analysis, patient records were de-identified and anonymized.

### Results

A total of 1615 case files were retrieved between the period of study. 497 case files were for pregnant women, 703 for children under the age of 18 years, while 15 case files had incompletely documented drug history information. 400 case files that met the inclusion criteria was reviewed and included in the study. The modal age group of PLWHA

**Table 1: Socio-demographic Characteristics of PLWHA attending ART Clinic in UITH**

Variable	Frequency (n=400)	Percentage (%)
<b>Age group (years)</b>		
18 – 30	88	22.0
31 – 40	120	30.0
41 – 50	97	24.3
51 – 60	51	12.7
≥ 61	44	11.0
<b>Gender distribution</b>		
Male	141	35.3
Female	259	64.7
<b>Marital status</b>		
Single	101	25.3
Married	164	41.0
Divorced	41	10.2
Widow	61	15.3
Widower	20	5.0
Separated	9	2.2
Undocumented	4	1.0
<b>Educational Status</b>		
None	56	14.0
Primary	69	17.3
Secondary	172	43.0
Post-secondary	103	25.7

**Table 2: Clinical Characteristics of PLWHA attending ART Clinic in UITH**

Variable	Categories	Present n (%)	Absent n (%)
History	Duration of the disease	388 (97.0)	12 (3.0)
	HAART Medications	400 (100.0)	0 (0)
	Other non-HAART Medications	103 (25.8)	297 (74.2)
	Duration on HAART	400 (100.0)	0 (0)
Physical Examination	Blood pressure	243 (60.8)	157 (39.2)
	Other findings (Oral thrush, Skin rash, Palor, Weight loss)	134 (33.5)	266 (66.5)
Result of Investigations	HIV screening	400 (100.0)	0 (0)
	HIV confirmatory test	400 (100.0)	0 (0)
	CD4 Count	347 (86.8)	53 (13.2)
	Viral load	378 (94.5)	22 (5.5)
	Full blood count	322 (80.5)	78 (19.5)
	Liver function test	257 (64.3)	143 (35.7)
	Electrolyte, urea, creatinine	281 (70.3)	119 (29.7)
	Lipid profile	194 (48.5)	206 (51.5)

**Table 3: Antiretroviral drugs prescribed to PLWHA attending ART Clinic and the frequency of prescription**

Antiretroviral drug Combinations	Number of patients	Total number of each HAART prescription	Percentage of each combination
Zidovudine/Lamivudine	11	248	5.8
Zidovudine/Lamivudine/Dolutegravir	18	477	11.2
Zidovudine	-	-	-
Atazanavir/Ritonavir	5	68	1.6
Lamivudine	-	-	-
Abacavir/Lamivudine	12	91	2.1
Abacavir/Lamivudine/Dolutegravir	35	152	3.6
Abacavir/Dolutegravir	13	103	2.4
Tenofovir/Lamivudine	71	640	15.1
Tenofovir/Lamivudine/Dolutegravir	284	1770	41.6
Tenofovir/Lamivudine/Efavirenz	3	42	1.0
Tenofovir-alafenamide/Lamivudine/Dolutegravir	1	18	0.4
Lopinavir/Ritonavir	12	135	3.2
Darunavir	-	-	-
Ritonavir	-	-	-
Darunavir/Ritonavir	-	-	-
Dolutegravir	62	465	10.9
Abacavir	-	-	-
Nevirapine	11	48	1.1
Raltegravir	-	-	-
Total		4257	100.0

attending ART clinic was 31 – 40 years (n=120, 30%), gender distribution showed that more female (n=259, 64.7%) were seen in the ART clinic. 41% of the patients were married and 1% did not have their marital status documented in the case note. About 43% had secondary school education, which constituted the largest

percentage (Table 1).

Most patient had the disease duration (97%), the different HAART combinations (100%) and duration on HAART (100%) documented. One-third had documentation of the physical examination findings (e.g oral thrush) and about two-third had their

**Table 4: Non-HIV medications prescribed to PLWHA attending ART clinic in UITH**

Medications	Number of patients	Total number of each non-HIV drug prescription	Percentage(%)
Anti-tuberculosis drugs	21	84	15.7
Cotrimoxazole	45	290	54.1
Analgesics	5	16	3.0
Fluconazole	7	12	2.2
Nystatin	3	8	1.5
Flucytosine	-	-	-
Amphotericin B	-	-	-
Traditional medications	-	-	-
Multivitamins/Iron Supplements	4	32	6.0
Anti-malarial drugs	12	16	3.0
Anti-diabetic drugs	3	37	6.9
Anti-hypertensive drugs	3	41	7.6
Total		536	100.0

blood pressure recorded. About a quarter had the documentation of the use of non-HIV medications (Table 2).

All the patient had HIV confirmatory test done before commencement of HAART while other necessary routine investigations like CD4 Count, Liver function test, kidney function test, and lipid profile were done only in 86.8%, 64.3%, 70.3% and 48.5% respectively (Table 2).

A total of 4257 prescriptions were evaluated and 20 different antiretroviral drug combinations were prescribed. The prescription pattern of the antiretroviral medication is as presented in Table 3. The most frequently prescribed combination was Tenofovir/Lamivudine/Dolutegravir (n=284, 41.6%) with a total of 1770 prescriptions. Majority (71.0%) received first line regimen and about a quarter (25.8%) were on non-HIV medications. Of the non-HIV drugs prescribed, Co-trimoxazole was the most prescribed and constituted 54.1%. Some patient (1.5%) had other chronic medical conditions like hypertension and diabetes mellitus for which they were using anti-hypertensive and anti-diabetic drugs (Table 4).

## Discussion

Pharmacotherapy constitutes over 90% of treatment modality in HIV/AIDS management.<sup>18</sup> PLWHA also have other medical diseases like hypertension and diabetes that will warrant the prescription and use of non-HIV drugs.<sup>19</sup> Proper evaluation and documentation of the drugs used by PLWHA is cardinal to the management of the patient, as this will mitigate against irrational prescribing, development of drug-drug interactions, adverse drug

reactions and possible treatment failure.<sup>20</sup> Our study revealed that about two-third of the people living with HIV/AIDS attending ART clinic in UITH were females and in their reproductive age. This finding was similar to the ones reported by Oreagba *et al*<sup>20</sup>, Furler *et al*<sup>21</sup> and Oku *et al*<sup>22</sup> by at variance with the one reported by Bersoff-Matcha *et al*<sup>23</sup>. With the finding that most of the patients were married and had secondary school level of education, it will be appropriate to incorporate HIV preventive measure and drug adherence into the counselling program. This program will help to improve compliance and reduce the transmission of the infection in the family and the society at large.

Majority of the patients had the duration of the disease, duration of the antiretroviral use and the different combinations of antiretroviral drugs in use documented in their case files. This finding is encouraging as it has epidemiological importance and can also help in patient evaluation and monitoring. The documentation of the use of non-HIV drug was poor (28.8%). It should be noted that just like any other patient, PLWHA can also develop other disease conditions like hypertension and diabetes which may necessitate the use of other medications. Nombela *et al*<sup>24</sup> in their study reported a fair documentation of the use of non-HIV drugs. The documentation of physical examination findings was found to be inadequate in this study. All patient should have a comprehensive general physical examination done as this may help to unravel the presence of other disease condition and also guide on the type of investigations and treatment. This finding is in support of the report by Sander *et al*<sup>25</sup> that the diagnosis of non-communicable diseases in low-income countries is not routinely performed during HIV visits. Justice *et al*<sup>26</sup>

reported a similar finding in their study while Marzolini *et al*<sup>27</sup> reported a different finding.

The importance of laboratory work up cannot be over-emphasized in the management of PLWHA. It guides the use of non-HIV medications and type of HAART combinations. The investigations to evaluate the replication and effect of the virus on the immune system were not in tandem with the guideline as between 5.5% - 14.0% did not have these investigations documented in their case file which is at variance with the recommendation by the international antiviral society.<sup>28</sup>

HIV and non-HIV drugs are metabolized by the liver and excreted by the kidneys; this makes it imperative to assess the clinical state of these vital organs in PLWHA. The organ specific tests (Liver Function Test, Electrolytes and Urea and Creatinine) were only done in 64.3% and 70.3% patient respectively. Patients with sub-clinical diseased organs who did not have the laboratory work up done may develop drug-drug interactions, adverse drug reactions and even therapeutic failure. All of these occurrences may mar the recent gains achieved in the treatment of HIV/AIDS.

Most of the patient seen in the ART clinic were on first line combination and the most frequently prescribed antiretroviral drug combinations was Tenofovir, Lamivudine, Dolutegravir. These combinations were alternative to the recommended first line regimen (AZT-3TC-EFV) though they are consistent with the WHO and National guidelines for the use of ARV drugs. The recommended EFV based first line combination were less frequently prescribed, we hypothesized that this may be due to intolerance to EFV and its contraindication in pregnancy as most of the patients were females, in the reproductive age group. Our study found the use of 20 different ARV drug combinations, this does not reflect rational prescribing and was in contrast to the guideline by WHO. Prescribers of antiretroviral drugs should be trained on the importance of rational prescribing particularly as it enhances adherence and reduces morbidity and mortality associated with irrational prescribing.

A quarter of the patient were found to be on non-HIV medications in this study. Tseng *et al*<sup>29</sup> in their study reported a higher proportion. Our findings on this were expected as physical examination and laboratory work up to diagnose the presence of non-communicable diseases are not routinely done. Of the non-HIV drugs prescribed, cotrimoxazole was the most commonly prescribed and the reason adduced for this was the fact that it is used in prevention of certain opportunistic infections like Pneumocystic Jiroveci Pneumonia and toxoplasmosis.<sup>30</sup> The cotrimoxazole chemoprophylaxis have been documented in literature to significantly reduce HIV related morbidity and

mortality.<sup>31</sup>

Some of the patients attending the ART clinic had pulmonary tuberculosis making the antituberculosis drugs the second most prescribed non-HIV medication in PLWHA attending the clinic. It should however be noted that this finding is contrary to the one reported by Mfinanga *et al*.<sup>32</sup> Contrary to the recommendation by WHO, it was noted that it is not all the patients with pulmonary tuberculosis that was on cotrimoxazole chemoprophylaxis. With our finding of antituberculosis drugs being the second most prescribed non-HIV drug, there should be increase surveillance for possible occurrence of drug-drug interaction as some of these drugs are either enzyme inducers or inhibitors.

### Conclusion

A number of PLWHA attending the ART clinic did not have a comprehensive physical examination documented in their case files. This may hinder the diagnosis of other disease conditions that might be present and needs medical treatment.

The documentation of the use of non-HIV medications by PLWHA was inadequate. This inadequacy can be minimized by training and re-training of doctors and prescribers on the importance of carefully documenting medications use by the patients as this will also impact positively and improve HIV care.

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