DRUG RELATED PROBLEMS ASSOCIATED WITH ANTI RETROVIRAL THERAPY OF HIV/AIDS PATIENTS AT NDOLA CENTRAL HOSPITAL

By

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A dissertation submitted to the University of Zambia in partial fulfilment of the requirements of the Degree of Master of Clinical Pharmacy

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CERTIFICATE OF APPROVAL

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DEDICATION

I dedicate this thesis to my husband, Mr Luke Banda, my children Zaweger Banda and Emmanuel Banda, my parents Mr Jonathan Munenu (Late) and Miss Dorothy Changwe for their love, support and patience during my studies.

ABSTRACT

Background: Antiretroviral therapy has posed multiple risks and challenges particularly in resource constrained African countries. This is due to the chronic nature of HIV/AIDS disease and hence its therapy, the use of combination therapy and also because therapeutic options and treatment guidelines continue to evolve. The increase in access to new essential medicines such as ARVs and the ARV regimen complexity and challenges increase the potential for drug related problems.

Objective: To determine the prevalence and patterns of drug related problems associated with anti-retroviral drugs in the management of HIV/AIDS patients at Ndola Central Hospital in 2016.

Methodology: A retrospective cross sectional study design involving 300 randomly sampled HIV positive patients admitted to the internal medicine wards of Ndola Central Hospital was conducted. The actual/potential patient specific ARV drug related problems were identified and classified according to the Pharmaceutical Care Network Europe (PCNE) V5.01 for drug related problems. The ARV drug classes associated with the drug related problems were also determined as well as the intervention rate against these drug related problems. This was achieved by review of patients' files and drug charts over a period of two months. The data from the research was analyzed using SPSS 20.0 version. Descriptive and inferential statistics such as frequency tables, percentages and chi square tests were performed.

Results: Out of 300 patients involved in the study, 31% had drug related problems associated with antiretroviral drugs in the management of HIV/AIDS patients. The prevalence of each Drug related problem in the management of HIV/AIDS patients were adverse drug event (40%), Non-compliance (40%) and no drug initiation (20%). Only the ARV drug class NRTIs, was significantly associated with adverse drug event and Noncompliance with p values= 0.03 and 0.011 respectively. The rate of intervention to prevent or resolve drug related problems associated with HIV/AIDS patients was 24 %.

Conclusion: The study revealed a high prevalence of DRPs with a risk of DRPs being high in patients taking NRTIs. The Antiretroviral drug related problems identified in the study were adverse drug event (40%), Non-compliance (40%) and No Antiretroviral drug initiation (20%). There was a low rate intervention in these DRPs and this can lead to the development of ARV resistance and treatment failure over time.

Key word: Drug related problems, Anti-retroviral drugs, HIV/AIDs.

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LIST OF ACCRONYMS AND ABBREVIATIONS

ADEs	Adverse Drug Events
ADR	Adverse Drug Reactions
AIDS	Acquired Immunodeficiency Syndrome
ART	Anti Retroviral Therapy
ARVs	Antiretroviral drugs
cART	Combined Anti Retroviral Therapy
DRP	Drug Related Problems
HAART	Highly Active Anti Retroviral Therapy
HIV	Human Immunodeficiency Virus
ME	Medication Error
NCH	Ndola Central Hospital
NNRTI	Non Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
PI	Protease Inhibitor
SPS	Strengthening Pharmaceutical Services
WHO	World Health Organization

DEFINITIONS

Adverse Drug Event: Injury resulting from appropriate/inappropriate use of a drug.

Adverse Drug Reaction: Any response to a medicine which is noxious, undesired and unintended drug effect which occurs at doses normally used in man for therapy, diagnosis or prophylaxis.

Co-morbidity: The presence of more than one disorder or illness in the same person.

Drug: A chemical substance that affects the processes of the mind or body and used in the diagnosis, treatment, or prevention of disease or other abnormal condition.

Drug interaction: When one drug alters the pharmacological effect of another drug. The pharmacological effect of one or both drugs may be increased or decreased, or a new and unanticipated adverse effect may be produced.

Drug Related Problem: An undesirable patient experience involving drug therapy that actually or potentially interferes with the desired patient outcome and requires clinical judgement to resolve.

Medication error: Any preventable event that may cause or lead to inappropriate medication use or patient harm while medication is in the control of the health care professional or patient or consumer.

Medication related illness: Same as Drug Related Problem.

Morbidity: The unhealthy state of an individual.

Mortality: Death.

Non-compliance: Failure by the patient to take the medicine as intended

Pharmacovigilance: The science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other possible drug-related problems.

Problem: In the phrase **"drug-related problem**" denotes a drug – related event amenable to detection, treatment, or more appropriately, prevention.

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CHAPTER ONE

BACKGROUND

1.1 Introduction

A Drug related problem (DRP) is an undesirable patient experience involving drug therapy that actually or potentially interferes with the desired patient outcome and requires clinical judgment to resolve (Cipolle *et al*, 2012; Molino *et al*, 2014). Drug related problems are harmful clinical events directly related to the use of medicines and may include under or over treatment, inappropriate dosing, adverse drug events, choice of formulation, drug interactions, poor adherence, and harm caused by adverse drug reactions (Strand *et al,* 1990; Cipolle *et al,* 2012 cited in Abah *et al*, 2014 p.3).

The burden of drug related problems on population health is high. WHO (2003, cited in Strengthening Pharmaceutical Systems (SPS) Program, 2011 p 24) estimates that worldwide more than 50 percent (%) of all medicines are prescribed, dispensed, or sold inappropriately, while 50% of patients fail to take their medicines correctly.

In developed countries, as many one in every 10 patients, are affected negatively by drugs when receiving hospital care (Adams et al, 2004). Although data is limited, the burden of DRPs is likely to be much worse in resource constrained African countries where there are weak health systems and shortages of trained health care workers.

HIV infected patients receiving highly active anti-retroviral therapy (HAART) are at increased risk of antiretroviral medication problems during hospitalization, due to the complexity of HAART regimens and the possibility of drug-drug interactions which may put patients at risk of toxicity or drug resistance (Heelon et al, 2007). Anti-retroviral therapy is complex and challenging because therapeutic options and treatment guidelines continue to evolve (Food and Drug Administration (n.d) quoted in Abah *et al,* 2014 p3). The chronic nature of HIV pharmacotherapy and the use of combination therapy, which includes the use of 3 or more antiretroviral drugs, as well as concomitant treatment of Opportunistic infections or non-communicable diseases, increase the potential for drug interactions and adverse drug reactions.

When part of the anti-retroviral regimen is missed or antiretroviral drug levels are low as a result of drug interactions or dosage errors, the virus can replicate and resistance to treatment can occur. Moreover, when an interaction leads to increased concentrations of anti-retrovirals in the body, or when a patient receives a higher dose than the correct one, toxicity can occur. Resistance or toxicity is more likely to take place when the drug related problem is extended in time or when the DRP is not resolved before the patients' discharge, since some medication problems may not have been resolved when the patients are discharged. A high level of adherence on a lifelong basis is required during therapy, which is also complicated by the possibility of serious side effects. If not used appropriately, the drugs are toxic and resistance may compromise the entire treatment (Giwa *et al*, 2011). The complex nature of the ARV therapy may lead to low adherence to ARV regimens which directly affects therapeutic efficacy (Molino *et al,* 2014). Treatment failure, which is commonly associated with resistance to ARV agents, increases as adherence to therapy decreases (Anderson *et al,* 2006 quoted in Molino *et al,* 2014, p 2). The ARV regimen complexity and challenges increase the potential for drug related problems (Ojeh *et al,* 2015).

Several studies have characterized the prevalence and nature of DTP and associated interventions in both hospitalized and ambulatory patients. Previous studies show that the prevalence of antiretroviral therapy (ART) administration DRPs in an in-patient setting range from 25.8% to 72% of admissions for patients on ART (Synder *et al,* 2011; Yehia *et al,* 2012; Merchen *et al,* 2011). A review of 25 studies conducted in 2014 shows a high incidence of 86% medications errors (DRPs) involving both antiretroviral (ARV) and opportunistic infection (OI) prophylaxis medications (Li and Foisy (2014)). Commonly identified errors being, omission of an ARV, inaccurate dosing frequency, or drug-drug interactions (Mok *et al*, 2008; Heelon *et al*, 2007; Rao *et al*, 2012; Corrigan *et al* 2010).

Literature is sparse on the burden of DRPs associated with ARVs in Africa; with the vulnerable population receiving treatment for HIV/AIDS and where most Cases of DRPs are not detected (SPS, 2011).

Therefore, the aim of this study is to identify the Drug-related problems associated with the management of HIV/AIDS and to determine the prevalence, risk factors as well as the drug

classes correlated with drug- related problems in hospitalized patients with HIV/AIDS at Ndola Central Hospital in 2016.

1.2 Rationale for the Study

DRPs need high attention as DRP related admissions with an average accounted for 8.36% in Europe (Conforti et al., 2012; Davies et al., 2010; Menéndez-Conde et al., 2011; Posthumus et al., 2012; Rodenburg et al., 2011; Singh et al., 2011; and Stausberg and Hasford, 2011).

With the growing number of HIV infected individuals accessing ARVs worldwide, the ever increasing HIV treatment options and ever changing treatment guidelines, understanding the nature and trend of DRPs is useful for the Ministry of Health in guiding intervention strategies to reduce DRPs.

The increase in access to new essential medicines such as ARVs demands a greater need to monitor for drug related problems and promote safety and effectiveness of medicines, particularly in Zambia, where, like many other African countries, the vulnerable population are receiving treatment for HIV/AIDS.

1.3 Study Justification

In developing countries, most cases of Adverse drug events (ADEs), adverse drug reactions and medication errors are not detected (Strengthening Pharmaceutical Systems (SPS) Program. 2011).

Scant data are available on the global burden of DRPs and ADRs associated with new medicines such as ARVs and there is increasing evidence on the surveillance of medicines related problems, particularly in Africa with the vulnerable population receiving treatment for HIV/AIDS (SPS Program, 2011).

The safety profiles of ARVs in developed countries may not necessarily be applied to other resource constrained settings like Africa where the incidence, patterns and severity of DRPs may

differ because of local, environmental and genetic influences (Pirmohamed *et al,* quoted in SPS, 2011, p21).

The study is important because it will provide information that can be used to make treatment guidelines to help minimize drug related problems associated with ARVs in the management of HIV/AIDS patients. The study will also propose a gap for further studies.

The study will also provide information on the need to monitor and promote safety and effectiveness of medicines in the management of HIV/AIDS patients.

1.4 Research Questions

1. What is the prevalence of each Drug related problem in the management of patients with HIV/AIDS?
2. What Anti-retroviral drug classes are associated with drug related problems in the management of patients with HIV/AIDS?
3. What is the rate of intervention to prevent or resolve DRPs in the management of HIV/AIDS?

1.5 Statement of the Problem

The scope of pharmacy practice now embraces more modern patient-focused and outcome-oriented pharmaceutical care than the traditional product-oriented roles such as compounding, supply and dispensing medications (Joda and Nwaokomah, 2011 cited in Oqua, *et al*, 2013). King and Fomundam, 2010 cited in Oqua, *et al,* 2013 p.2) describe Pharmaceutical care as the responsible provision of medication-related care in order to achieve definite outcomes that improve a patient's quality of life.

WHO (n.d cited in Strengthening Pharmaceutical Systems (SPS) Program, 2011) estimates that worldwide more than 50 percent (%) of all medicines are prescribed, dispensed, or sold inappropriately, while 50% of patients fail to take their medicines correctly.

In Africa—4.5–8.4% of all hospital admissions were related to ADRs, 1.5–6.35% of patients were admitted as a direct result of ADRs; and 6.3–49.5% of all hospitalized patients developed ADRs. Moreover, 45% of ADRs accounted for the most frequent reason for treatment modification and interruptions in patients on ART (Tumwikirize, 2011; Jaquet, 2011 cited in Strengthening Pharmaceutical Systems (SPS) Program, 2011).

No study has been documented in Zambia to determine the burden of drug related problems in anti-retroviral therapy.

If the current scenario continues, antiretroviral therapeutic switches may ensue, leaving fewer alternative treatment options for future switches, leading to the use of more expensive regimens, which in turn escalates the cost of health care delivery. Also, resistance to ARVs and other drugs used to treat opportunistic infections may occur with resultant poor treatment outcomes or even death. Ultimately, loss of confidence in the health system by patients takes place (Strengthening Pharmaceutical Systems (SPS) Program. 2011).

A study by Abah *et al,* 2014 in Nigeria documented the patterns of drug related problems as an untreated indication (49.3%) as the most common type of DRP, such as failure to initiate ART when eligible or suboptimal treatment for hepatitis B co-infection. This was followed by therapeutic failure (25.9%) and drug toxicity (22.9%).

The United States of America (USA) estimated that ADEs are the fourth to sixth leading cause of death. Also, the contribution of ADEs to the cost of the health system is estimated at $177.4 billion in 2000, which is huge (Strengthening Pharmaceutical Systems (SPS) Program. 2011). Literature is sparse on studies evaluating DRPs in the management of HIV/AIDS and the impact on ARV resistance and adherence to treatment in sub-Saharan Africa.

In developing countries, most cases of Adverse drug events (ADEs), adverse drug reactions and medication errors are not detected.

Scant data are available on the global burden of DRPs and ADRs associated with new medicines such as ARVs and there is increasing evidence on the surveillance of medicines related problems, particularly in Africa with the vulnerable population receiving treatment for HIV/AIDS (Strengthening Pharmaceutical Systems (SPS) Program. 2011).

The current authors have recommended further studies to determine the burden of DRPs associated with ARVs particularly in Africa (Strengthening Pharmaceutical Systems (SPS) Program (2011).

Therefore, the purpose of this cross sectional study was to identify and determine the patterns and prevalence of drug related problems associated with ARVs in patients with HIV/AIDS admitted at the Ndola Central Hospital in 2011.

1.6 Objectives

1.6.1 Main Objective

To determine the patterns and prevalence of drug related problems associated with ARVs in hospitalized patients with HIV/AIDS at Ndola Central Hospital in 2016.

1.6.2 Specific objectives

1. To determine the prevalence of each Drug related problem associated with ARVs.
2. To identify the Anti-retroviral drug classes associated with Drug related problems in HIV/AIDS patients.
3. To evaluate the rate of interventions to prevent or resolve Drug related problems associated with HIV/AIDS patients.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

Literature Review will focus mainly on the following objectives of this study:

1. To determine the prevalence of each Drug related problem associated with ARVs.
2. To identify the ARV drug classes associated with Drug related problems in HIV/AIDS patients.
3. To evaluate the rate of interventions to prevent or resolve Drug related problems associated with HIV/AIDS patients.

2.2 Classification of Drug related problems

A rational, safe and cost effective drug treatment depends on competent diagnosing, prescribing, effective monitoring and evaluation of drug therapy, patient understanding and compliance with regards to the prescribed medication. Identification and resolving the drug related problems in the prescriptions is the core activity in pharmaceutical care and therefore suitable classification of DRPs is relevant in pharmaceutical care practice and research. Eight different categories of DRPs are described in the classifications of DRPs. This categorization serves a number of functions which include: 1) to illustrate how adverse drug reactions form, but one category of extant DRPs; 2) to make the roles of a pharmacist tangible in the future; 3)to serve as a focus for developing a systematic process whereby the pharmacist contributes significantly to the overall positive outcome of the patients; 4) to bring to the pharmacy practice a consistent vocabulary with other health care professionals; and 5) to aid the development of standards of practice for pharmacists (Adusumilli and Adepu (2014)).

Different DRP classification systems, each with a different focus, are published in the literature in various international journals and about fourteen different classifications on DRPs were found published. Some classifications were hierarchical, categorized into main groups and subgroups with various terminologies and definitions for DRPs (Adusumilli and Adepu (2014)).

These classifications of DRPs include: 1) The ABC of DRPs-, Meyboom *et al*. in 2000 published a basic system for DRPs seen from a pharmacovigilance viewpoint primarily for use in the WHO and focuses on side effects and adverse reactions. Each category has its own definition, but a general definition for DRPs was not given, 2) American Society of Hospital Pharmacists (ASHP) classification 1996 -DRPs were then defined as "medication-therapy problems." In 1998, they defined medication-related problem as "…an event or circumstance involving medication therapy that actually or potentially interferes with an optimum outcome for a specific patient" (Adusumilli and Adepu (2014)).

3) Cipolle/Morley/Strand classification- "drug-therapy problem" rather than "DRP." The concept generally refers to a system approach, including problems in the whole drug therapy chain, from the patient's perspective, published in 1999. Definition: Any undesirable event experienced by the patient that involves or is suspected to involve drug therapy and that actually or potentially interferes with a desired patient outcome, 4) Granada consensus-in 1998 a group Spanish experts defined DRPs as: Drug Therapy Problems are health problems, understood as negative clinical outcomes, resulting from pharmacotherapy that for different causes, either do not accomplish therapy objectives or produce undesirable effects, 5) Hanlon approach- Hanlon *et al*. developed a method for assessing the appropriateness of medication based on the medication appropriateness index (MAI) but no definition was given (Adusumilli and Adepu (2014)).

6) Hepler–Strand classification- With their seminal publication on pharmaceutical care, Hepler and Strand also introduced several categories of DRPs with the following Definition: An event or circumstance involving a patient's drug treatment that actually or potentially interferes with the achievement of an optimal outcome. 7) Krska *et al*. system- Krska *et al*. developed a classification based upon the DRPs they encountered during a research project based upon drug-use evaluation. 8) Mackie classification- according to Mackie, a clinical DRP is considered to exist when a patient experience or is likely to experience either a disease or symptom having an actual or suspected relationship with drug therapy. Mackie et al adapted the Cipolle *et al*. classification based upon their own findings on a random sample of 50 patients with one or more DRPs (Adusumilli and Adepu (2014)).

9) National Coordinating Council for Medication Error Reporting and Prevention (NCC-MERP) taxonomy of medication error- defines DRP as preventable event that may cause or lead to inappropriate medication use or patient harm, whereas the medication is in control of the health care professional, patient, or consumer. 10) PAS coding system- originally was developed to document patients' questions on their drug therapy, not to classify DRPs. 11) Pharmaceutical Care Network Europe (PCNE) system (version 4.0) - created in 1999 by pharmacy practice, researchers during a working conference of the PCNE in an effort to develop a standardized classification system that is suitable and comparable for international studies. According to PCNE classification system, a DRP is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes (Adusumilli and Adepu (2014)).

12) Problem–intervention documentation (PI-Doc) - this hierarchical system for PI-Doc was developed in Germany with an emphasis on the user-friendliness in community pharmacy practice. 13) SHB-SEP classification- The Health Base Foundation developed this system in The Netherlands for use in pharmacy software's based upon the medical Subjective/ Objective/Evaluation/Plan structure; however, the S and O codes have been combined into one problem description and 14) Westerlund system- was developed as part of a PhD thesis and was first used in 1996. Definition: DRP is a circumstance related to the patient's use of a drug that actually or potentially prevents the patient from gaining the intended benefit of the drug (Adusumilli and Adepu (2014)).

Therefore, summating different authors' opinions, DRPs may be defined as "an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes". For the purpose of this study, the Pharmaceutical Care Network Europe (PCNE) system (version 5.01) was adopted (Adusumilli and Adepu (2014)).

2.3 Prevalence of Drug related problems associated with ARVs

Hamid *et al* (2014) defined prevalence of DRPs as the number of patients or hospital admissions with at least one (1) DRPs (numerator),divided by the total number of patients or hospital admissions included in the study (denominator).

A number of studies have documented the prevalence of ART administration DRPs in an inpatient setting as ranging from 25.8% to 72% of admissions for patients on ART (Synder *et al,* 2011; Yehia *et al,* 2012; Merchen *et al,* 2011).

Yehia *et al* (2012) conducted a study in the USA entitled 'Antiretroviral Medication Errors Remain High but are quickly corrected Among Hospitalized HIV infected Adults. A retrospective review of medication orders involving 388 patients during the first 48 hours of hospitalization for HIV-infected patients admitted to the Johns Hopkins Hospital between January, 2009 and December 31, 2009 was conducted and found that 29% of hospitalizations had an antiretroviral prescription error (DRP) on the first day of admission, which decreased to 7% by hospital day 2. The study concluded that ART Medication Errors (DRPs) are common among hospitalized HIV patients on the first day of admission, but are corrected within 48 hours. The study only evaluated patients enrolled in the Johns Hopkins HIV Clinical Cohort (JHHCC) but did not review records of hospitalized patients with HIV receiving care at outside institutions. Though a high prevalence of drug related problems was reported, this could have affected the result.

Another study was conducted in USA by Commers *et al* (2013) with the main objective being to determine whether Errors in prescribing Antiretroviral therapy often occur with the hospitalization of HIV-infected patients; The rapid identification and prevention of error may reduce patient harm and health care costs. A retrospective medical record review of hospitalized HIV-infected patients was conducted between January 1, 2009 and 31 December 2011. Out of 416 hospital admissions included in the study, 35.1% had ART errors (DRPS). The study concluded that Errors (DRPS) in ART in-patients were common and the majorities were never detected.

A retrospective, observational, electronic medical chart review of 344 patients with HIV/AIDS admitted between February 15, 2011- May 22, 2012 was conducted in the United States by Champias *et al* (2015) to evaluate the occurrence and type of antiretroviral and opportunistic infection medication error (DRP) within the inpatient setting. The study showed that the overall prevalence of ARV DRPs was 35%. The study concluded that Errors (DRPs) relating to ARV and OI medications are frequent in HIV-infected inpatients. The study excluded patients not receiving or refusing ARV and/or OI medications, or newly diagnosed and hence missed the chance to assess DRPs in terms No drug initiation when the patients were eligible. The study also looked at drug-drug interactions involving ARVs as a separate entity and not as part of the Errors (DRP) reported. This reduced the prevalence of DRPs recorded as the study reported that 9% of the patients enrolled in the study experienced drug interactions. Therefore, the prevalence of drug related problems would have been higher than what was reported.

Lauzevis *et al* (2013) conducted a study entitled 'Evaluation of a strategy aimed at reducing errors in antiretroviral prescriptions for hospitalized HIV-infected patients'. The study aimed to evaluate the prescription of antiretroviral drug regimens at hospital admission and the impact of strategies implemented to prevent errors. The study included HIV infected patients managed by the hospital as outpatients and admitted between January 1, 2010, and December 31, 2010 (first period) and between February 1, 2011, and January 31, 2012 (second period). The study identified 39% of medication- related error (DRPs) during the first period and 42% during the second period. The study concluded that errors (DRPs) made in the prescription of antiretroviral medication were frequent and interventions allowed to correct 36% of errors. Other strategies like consulting a clinical pharmacist on admission, or training prescribers should be considered.

Carcelero *et al*, (2011), conducted an observational, prospective, 1-year study in a 750-bed tertiary-care teaching hospital in Spain by a pharmacist trained in HIV pharmacotherapy with the aim of identifying antiretroviral-related errors in the prescribing of medication to HIV-infected inpatients and to ascertain the degree of acceptance of the pharmacist's interventions. The study found the prevalence of antiretroviral related problems to be 21.7%. The study concluded that Errors in, or problems with, the HAART regimen were common among HIV-infected hospitalized patients prescribed antiretroviral agents (approximately one-in-five patients).   The

study did not assess dispensing or administration errors, or the clinical outcomes of the interventions (prevention of drug toxicity or drug resistance).

Eginger *et al* (2013) conducted a study involving 86 patients to assess the impact of pharmacist interventions on the rate of medication error (DRPs) in HIV infected hospitalized patients who had been prescribed HAART in the outpatient setting. Out of the patients receiving HAART and/ or Opportunistic (OI) prophylaxis, 54.7% had at least one (1) medication error (DRP) on admission. The study concluded that a clinical pharmacist's targeted review of outpatient prescribed HAART and/or OI primary prophylaxis regimens on hospitalized HIV-infected patients can reduce most medication errors during hospitalization. The sample size was too small to enable generalization of the study findings to other institutions.

The variation in the prevalence of DRPs between studies could be due to the following reasons: (i) the definition and methods used to identify the DRPs; (ii) the heterogeneous estimates of the reported prevalence, and (iii) the risk factors associated with these DRPs.

Therefore, for the purpose of this study, DRPs will include all aspects of DRPs (ADEs, ADRs and ME), which include the following: drug omission, unnecessary drug, wrong drug indication, an incorrect dose, dose omission, drug-drug interactions, non-compliance, therapeutic failure, and drug toxicity (adverse drug reaction). The documented prevalence of DRPs in all the above studies is high regardless of the value, and the goal for all institutions should be no drug related problems.

2.4 ARV Drugs/Classes used in the management of HIV/AIDS

The Food and Drug Administration (FDA) approved more than 25 antiretroviral drugs in 6 mechanistic classes. The six classes include the Nucleoside/Nucleotide Reverse transcriptase inhibitors (NRTIs), non –Nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), a Fusion inhibitor (FI), a CCR5 antagonist, and integrase strand transfer inhibitors (INSTIs). In addition, ritonavir (RTV or r) and cobicistat (COBI or c) are used solely as pharmacokinetic (PK) enhancers (boosters) to improve the pharmacokinetic profiles of some ARV drugs (e.g., PIs and the INSTIs elvitegravir (EVG)).

The initiation of antiretroviral therapy for a treatment- naïve patient generally consists of two NRTIs, usually Abacavir/ Lamivudine (ABC/3TC) or tenofovir disproxil fumarate/Emtricitabine (TDF/FTC), plus a drug from one of the three drug classes: an INSTIs, an NNRTIs, or a PK-enhanced PI. All recommended and alternative regimens include an NRTI combination of Abacavir/Lamivudine or Tenofovir/Emtricitabine, each of which is available as a fixed-dose combination tablet. The choice of NRTI combination is usually guided by differences between Abacavir and tenofovir, because Emtricitabine and Lamivudine have fewer adverse events and comparable efficacy. The main advantage of tenofovir over Abacavir is its activity against hepatitis B virus (HBV), so relevant in hepatitis B co-infected patients, and the fact that HLA-B5701 testing is not required for its use. The main advantage of abacavir over tenofovir is that it does not require dose adjustment in patients with renal insufficiency and has less nephrotoxicity and less deleterious effects on bone mass density than tenofovir. However, the use of Abacavir has been linked to cardiovascular events, in some, but not all, observational studies.

The choice between an INSTI, NNRTI, or PI as the third drug in an initial regimen must be guided by the regimen's efficacy, genetic barrier to resistance, adverse effects profile, and convenience. The patient's co-morbidities, concomitant medications, and the potential for drug-drug interactions should be also considered. The recommended regimens include an INSTI or DRV/r in combination with 2 NRTIs. For most patients, an INSTI-containing regimen will be highly effective, have few adverse effects, and (with RAL and DTG) have no significant CYP 3A4-associated drug interactions.

Alternative regimens include either an NNRTI-based (EFV or RPV) or a pharmacokinetic-enhanced, PI-based (Atazanavir/r, Atazanavir/cobicistat or DRV/c) regimen. NNRTIs (EFV or RPV) are optimal choices for some people, even though they have low genetic barriers to resistance, especially in patients with suboptimal adherence. Most EFV-based regimens have a strong virologic efficacy, including patients with a high HIV-RNA (except when EFV is used with ABC/3TC); however, the relatively high risk of CNS-related side effects makes the EFV-based regimen less tolerable than other regimens.

2.5 Patterns of Drug related problems associated with ARVs

Drug related problem (DRP) is an undesirable patient experience involving drug therapy that actually or potentially interferes with the desired patient outcome and requires clinical judgement to resolve (Cipolle *et al*, 2012;Molino *et* al, 2014)). Drug related problems are harmful clinical events directly related to the use of medicines and may include under or overtreatment, inappropriate dosing, adverse drug events ,choice of formulation, drug interactions, poor adherence, and harm caused by Adverse drug reactions (Strand *et al,* 1990; Cipolle *et al,* 2012 cited in Abah, 2014 p.3).

Several studies reported, and described different patterns of drug therapy problems associated with HIV /AIDS management.

A study done by Yehia *et al* (2012*)* went further to determine the patterns of DRPs and classified the DRPs as: 1) incomplete regimen; 2) incorrect dosage; 3) incorrect schedule; and 4) non-recommended drug-drug combinations (drug interactions). All the data were abstracted from the JHHCC database, except for inpatient medication orders that were obtained from comprehensive Johns Hospital inpatient pharmacy and billing system. The study recorded the most common DRPs as incomplete regimen (58%), followed by incorrect dosage (38%), incorrect schedule (23%) and non-recommended drug-drug combinations.

Snyder *et al* (2011) conducted an in-depth analysis of medication errors (DRPs) in hospitalized patients with HIV with the main objective to determine the incidence of combination antiretroviral therapy (ART) and opportunistic infection (OI)-related medication errors and to describe the nature and cause(s) of errors to guide future interventions. A prospective review of 26 patient charts, medication profiles, and medication administration records for medication errors (DRPs) such as improper dosing, interactions, drug omissions, and missing doses for patients admitted to a tertiary care teaching hospital during 2 consecutive months in 2005. The study identified 77% of combined ART – and OI – related medication error (DRPs) and concluded that a prospective investigation of medication error (DRPs) provided in depth insight into the diverse nature of HIV-related medication errors, risk factors, and potential preventive strategies.

Ojeh *et al* (2015) conducted a prospective pharmacists' intervention study on 9339 HIV patients between January and August 2012 at the outpatient HIV clinic of the Jos University Teaching Hospital (JUTH). The study aimed to describe the frequency and types of drug therapy problems (DTPs), and interventions carried out to resolve them, among a cohort of HIV-infected patients on ART in Jos, Nigeria. The study shows that the most common type of DRPs was drug omission (21.7%), followed by unnecessary drug (13.1%) and wrong drug indication(13.1%) respectively. The findings of the study suggest that pharmacists-initiated interventions can ameliorate DTPs in patients receiving ART, given the high intervention acceptance rate recorded. The implication of this finding is that pharmacists with requisite training in HIV pharmacotherapy are an excellent resource in detecting and minimizing the effect of antiretroviral drug-related errors.

Abah *et al* (2014) prospectively conducted a 1year descriptive study (case series) on 9320 patients in Nigeria from July 2010 to June 2011 at the adult HIV clinic of Jos University teaching Hospital. The study documented the most common type of DRP as an untreated indication (49.3%), such as failure to initiate ART when eligible, followed by therapeutic failure (25.9%) and drug toxicity (22.9%). The study, however, was not able to determine the impact of pharmacist's intervention on drug resistance.

Carcelero *et al* (2011) went further to identify the drug related problems and documented that the most common was drug–drug interaction (33.3%), not only between antiretroviral agents, but also between antiretrovirals and other drugs. Atazanavir was the drug most commonly involved in interactions. The second most common problem was incorrect dose (16.7%), and the third most common was dose omission (15%), followed by lack of dosage reduction in patients with renal or hepatic impairment (11.7%), omission of one or more antiretroviral medications (10%), addition of an alternative antiretroviral drug (8.3%) and incorrect schedule according to outpatient treatment (5%). Inpatient antiretroviral prescriptions were compared with outpatient dispensing records for reconciliation. Renal and hepatic function was monitored to determine the need for dose adjustments.

Lauzevis *et al* (2013) also determined the patterns of drug related problems. The study retrospectively identified errors made in the prescription of antiretrovirals by comparing the

drugs prescribed during hospitalization and those documented in the outpatient file. During the second period, the study implemented a strategy involving the pharmacist and the infectious disease specialist to reduce the number of errors (DRPs). The most common errors (DRPs) documented were drug omission, inappropriate dosage, or failure to adjust dosage for renal insufficiency.

Molinio *et al* (2014) conducted an 18-month prospective controlled study, in which 90 outpatients were selected by convenience sampling from the Hospital Dia–University of Campinas Teaching Hospital (Brazil). Forty-five patients comprised the pharmacist intervention group and 45 the control group. All the patients had HIV infection with or without acquired immunodeficiency syndrome. The study evaluated the impact of pharmacist interventions on CD4+ T-lymphocyte count, HIV viral load, and DRPs in patients with HIV infection. The study found that adverse drug reactions were the most prevalent DRPs. The study suggests that pharmacist interventions in patients with HIV infection can cause an increase in CD4+ T-lymphocyte counts and a decrease in DRPs, demonstrating the importance of an optimal pharmaceutical care plan.

A study by Eginger et al (2013) further investigated the patterns of DRPs involved with HAART and/or OI prophylaxis. The study documented that Dose omission (45.5%) was the most common error type among HAART and/or OI prophylaxis regimen, followed by incorrect regimen (17.1%) and incorrect dose (15.1%).

Li and Foisy (2014) conducted a study on Antiretroviral and medication errors in hospitalized HIV-positive patients with the main objective of summarizing the literature regarding antiretroviral and other medication errors in hospitalized HIV-positive patients and to discuss potential interventions and solutions that have been studied to minimize drug error. A systematic search of MEDLINE, Pubmed and EMBASE (2000-April 2014) on English –Language research articles, case reports, conference abstracts, and letters to the editor were reviewed. The most common Errors (DRPS) in the antiretroviral regimen were dosing, scheduling, and drug-drug and drug food interactions. The study concluded that although studies varied greatly in methodology, overall, a large number of medication errors (DRPs) occurred in this patient population.

The definitions of DRPs may influence the patterns of DRPs identified in various studies. The following are the subgroups of DRPs: adverse drug events (ADEs), adverse drug reactions (ADRs) and Medication errors (MEs) (Leendertse *et al*, 2008), quoted in Hamid *et al*, 2014 p2). An ADE is defined as the injury resulting from the appropriate/inappropriate use of a drug (Hardmeier *et al,* 2004, quoted in Hamid *et al,* 2014, p 2). Medication error is defined as 'any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional or patient or consumer'(NCCMERP, 2013). ADR is defined as any response to a medicine which is noxious, undesired and unintended drug effect which occurs at doses normally used in man for therapy, diagnosis or prophylaxis (WHO, 2011). Some studies may have used only one or two of the subgroups of DRPs. The mode of data extraction to identify DRPs can also affect the patterns of drug related problems in that prescriptions may not capture patient characteristics such compliance to ARV medication, CD4 count to determine eligibility to initiate ART, patients renal function status to determine the correct ARV or the dose of ARV to give. Our study therefore adopted the review of patients Files and charts which capture all forms of DRPs.

The fact that NRTIs are often the 'backbone' of the cART makes them the most frequently prescribed class of ARVs. The dosing of PIs is complicated and boosting with ritonavir is required for almost all PIs, which confuses those unfamiliar with the drugs. Thus, the two classes being the most involved in DRPs (Chiampas *et al,* 2015).

The safety profiles of ARVs in developed countries may not necessarily be applied to other resource constrained settings like Africa where the incidence, patterns and severity of DRPs may differ because of local environmental and genetic influences (Pirmohamed *et al,* quoted in SPSS, 2011, p21). The patterns of DRPs identified in the management of HIV/AIDS in the studies may differ due to ever changing treatment guidelines. In summary, the differences in the patterns of DRPs in the various studies are due to the fact that the causes of DRPs are multifactorial (Champias et al, 2014).

2.6 Association between ARV Classes and Drug related problems in HIV/AIDS patients.

A study done by Commers *et al* (2013) to quantify and characterize ARV related medication errors on hospital admission at the teaching hospital of the university of Nebraska medical Center (UNMC) in USA, also set out to determine whether a particular ARV drug class was associated with an increased risk of prescription error (DRP). The findings of this study show that PIs were not associated with an increased risk of prescribing error (DRP). However, NRTIs were associated with a high risk of prescribing error (DRP).

A study done in Kenya by Arika (2011) documented that parents that were on ART was significantly associated with adherence (noncompliance). The study further determined a statistically significant association between caregivers difficulty in adhering to own ARV medication and child's adherence/non-adherence outcome with a p<0.05.

Champias *et al* (2015), however, found no statistical association between a specific ARV class and a specific DRP.

2.7 Intervention rate to prevent or resolve Drug related problems associated with HIV/AIDS patients.

Interventions/actions taken to prevent or resolve DRPs are defined as measures taken by the patient and medical team to resolve or prevent DRPs and to encourage the adoption of healthy habits (quality of life intervention)(Molino *et al,* 2014). Interventions towards DRPs include guiding patients mainly regarding adherence (compliance) to the prescribed therapeutic regimens and medication changes by physicians when needed. Other interventions include changes in case of problems with dosage, drug-drug and drug-food interactions, side effects and adverse drug reactions (Molino *et al,* 2014).

The percentage of patients with DRPs and were provided interventions during the study period was calculated as the "number of patients provided DRPs interventions during the study period divided by the number of patients who were documented to have DRPs during the study period x100" (Agu *et al,* 2014).

A study by Agu *et al* (2014) documented that 98.3% of participants who had medication errors (DRPs) received interventions for the medication errors and 97.4% of the potential/actual DRPs were resolved.

Another study by Chiampas *et al* (2015) observed that documented correction of DRPs for the clinical specialist was approximately 50%.

Carcelero *et al* (2011) documented a 100% intervention in all the 60 DRPs detected.

Abah *et al* (2014) in a study entitled "Pharmaceutical Care Outcomes in an outpatient immunodeficiency virus treatment Centre" aimed at describing changes in clinical end points (viral load, CD4 Count and ARV toxicity-related Laboratory evaluations) that occurred after intervention by a pharmacist among patients on ART. The study documented a 0.9% intervention rate of the population seen during the study period. The study concluded that though the Pharmacist's rate of intervention was low in the study, the study was still able to describe several important DRPs among HIV infected patients in whom favorable virological and immunological outcomes post-Pharmacist intervention were observed. The study by Abah *et al* (2014) surprisingly documented a low intervention rate, although it involved the intervention of a Pharmacist. This phenomenon may be attributed to many factors such as a high patient burden and under-reporting of interventions due to inadequate time during the clinic to document each intervention. Under-reporting of interventions may also be due to the fact that only interventions accepted by the attending physician were documented. Besides, only interventions of greatest clinical importance and those most likely to result in favorable HIV clinical outcomes were documented in the study.

It is difficult to compare the actual DRPs interventions for various studies due to variability in the interventions and data collection.

In a study by Abah *et al* (2014), DRPs interventions resulted in medication changes to resolve the DRPs including an ARV drug substitution to a safer first-line drug (33.8%), a switch from

first to second-line ART (23.5%), and ART initiation (24.7%). Other actions taken included the addition of a new drug (8.2%); drug discontinuation (2.4%); and dosage adjustment or adherence counseling (1.2%). HIV clinical specialists (Pharmacists and physicians) with training in HIV pharmacotherapy can play an important role in correcting DRPs (Carcelero *et al*, 2011).

CHAPTER THREE

METHODOLOGY

3.1 Introduction

The main concerns of the study included the identification of the actual/potential patient-specific drug related problems, the drugs involved in these drug related problems and the intervention rate against DRPs.

3.2 Study Design

The study was designed as a retrospective cross sectional study based on objective 1 and 3 as it aimed at just describing the trend of the drug related problems and the intervention rate towards these drug related problems.

3.3 Study Setting

The study was carried out at Ndola Central Hospital, Zambia. Ndola Central Hospital is a public tertiary hospital located in the Copperbelt Province of Zambia. As of July, 2016, 7163 active clients and a total of 13052 clients have ever been on ART, accessing ART services in the outpatient clinic, with the attrition rate of 45.1%.

The study was conducted in the Department of Internal Medicine and Admission ward. The following comprise the Internal Medicine wards: Male Medical Ward West, Male Medical Ward East, Female Medical Ward West and Female medical Ward East. The four Medical Wards have a bed capacity of 214 beds in total, distributed as follows: FMWW - 48; FMWE – 50; MMWW - 56; MMWE – 60. The wards also accommodate extra floor beds when the actual beds are filled to capacity.

3.4 Duration of the study

Data was collected over a period of 2 months, from June to July, 2016.

3.5 Data source and study population

The study involved a review of patient files and drug charts to assess the occurrence and type of DRPs. Information on current Medication was obtained from the patients' Charts while that of

past Drug history, diagnosis, symptoms/complaints/causes of hospitalization was obtained from the patients' files.

A pharmcotherapeutic team consisting of a Pharmacist (researcher), a senior Registrar and consultant physician in Medicine reviewed data and established the causal relationship between the drug and subsequent problem. The researcher then recorded the interventions conducted by the physicians to prevent the potential DRP or resolve the actual DRP.

Eligibility for Antiretroviral therapy was determined based on Zambia Consolidated Guidelines for Treatment and Prevention of HIV Infection (2014) which recommends initiation of ART in Adolescent/adult ≥15 years old with CD4 count ≥500 cells/ml and WHO Stage 1 or 2, WHO Stage 3 or 4, HIV-TB co-infection, HIV-HBV co-infection.

3.6 Inclusion criteria

- Patients with HIV/AIDS on HAART or Eligible for HAART.
- All patients aged above18years with a length of hospital stay ≥24 hours
- Patients must be admitted to the admission and Internal Medicine wards of NCH.
- Files of patients admitted to the admission and Internal Medicine of NCH.

3.7 Exclusion criteria

- All other patients
- Obese patients because some ARVs can cause obesity.
- Cases involving drug abuse, alcoholism, suicide attempts.

3.8 Sample size determination

At 95% confidence level and a Prevalence of 72%, according to a study done by Synder *et al* (2011); Yehia *et al* (2012); Merchen *et al* (2011) and a precision of ±5%, a sample size was calculated as follows:

$$n = \frac{Z^2 P (100-P)}{e^2}$$

Where n is the sample size;

P is the prevalence 72%;

Z (1.96) is area under curve for confidence level of 95% and

e is the marginal error which is 5 in this case.

Therefore n= 1.96^2 X 72 (100-72)/5^2 = **310.**

3.9 Sampling Method

The patients' files were sampled using a simple random sampling method. A list of numbers was entered in the Excel spreadsheet for all the files that met the inclusion criteria for the period under review. Then, in the column right next to the list, the function=RAND ( ) was pasted. This is an EXCEL's way of putting a random number in the cells. Then, sorted the column with a list of file numbers, this rearranged the list in random order from the lowest to the highest column number. Then, the first 310 files were isolated for review.

The study sample was from one sample frame: Patients' records.

3.10 Variables

Table.3.1: Types of variables and their definitions.

Variable Name	Definition	Type of Variable	Scale of Measurement
Prevalence **each** of DRP in HIV	Number of patients with at least 1 specific type of DRP (numerator) divided by the total number of patients with drug related problems included in the study (denominator) admitted to internal Medicine and admission wards of NCH.	Categorical	Frequency
DRP	Drug-related problems will be defined as Adverse drug reactions, non-compliance, sub-	Categorical 1=under treatment 2=overtreatment 3=non-compliance 4=adverse drug	Frequency

	therapeutic dose, supra-therapeutic dose, drug-interactions., according to Pharmaceutical Care Network Europe V5.01 of 2006 (Appendix A).	reaction, etc.	
Drugs associated with drug-related problems	Drugs will be grouped as drug classes according to their mechanism of actions as outlined in the British National Formulary (BNF) e.g., ARV classes such as Nucleoside Reverse Transcriptase Inhibitors (NRTIs), Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs), Protease Inhibitors (PIs), Fusion Inhibitors and other drug classes used to treat other co-morbidities will be grouped together as other drugs.	Categorical 1=Nucleoside Reverse Transcriptase Inhibitors 2=Non-Nucleoside Reverse Transcriptase Inhibitors 3=Protease Inhibitors 4=Fusion inhibitors.	Frequency

Actions/Intervention(rate) to prevent or resolve DRPs	The percentage of patients with DRPs provided with interventions during the study period will be calculated as the "number of patients provided DRPs interventions during the study period divided by the number of patients who were documented to have DRPs during the study period x100"	Categorical 1=drug stopped 2=Additional drug given 3=dose of drug reduced 4=drug changed, etc.	Frequency

The drug regimens that were assessed include 1st and 2nd line treatment regimens for HIV/AIDS which Ndola central Hospital offers.

The study only focused on drug related problems associated with ARVS.

3.11 Data collection

Initial screening, was carried out by the researcher for each ward , recording demographic details, presenting complaints, diagnosis, disease states, drug therapy at the time the patient was enrolled in the study. Data was abstracted from patients' records (files and charts) and will include laboratory results during admission.

If there were any uncertainties about information in the medical records, extra information was obtained from care providers involved. Patients were not interviewed. The patients/records were given codes and the gender and age of the patients were noted.

All information for each suspected DRP was collected by the researcher and was presented in the form of an individual case review. Review of files was done twice a week for each patient included in the study as some patients develop DRPs during their stay in the Hospital. The case review was reported based on information obtained from the case notes, medication chart and nursing notes. The case reviews were then sent in batches to each member of the reviewing panel

(pharmacotherapeutic team). Varying numbers of patients (one to three) considered not to have a DRP will be included in each batch of 25 case reviews.

Two of the three reviewers were blind to the DRP/non DRP status of cases.

Each panelist reviewed the cases independently of the other panel members. For each patient, the reviewer decided whether a DRP exists definitely, possibly or not at all. They then classified the DRP and then associated the drug(s) to the subsequent DRP. The researcher then recorded the rate of action or Intervention undertaken in order to prevent or resolve such a DRP.

A causal relationship between a suspected drug and a DRP was also established as definite, probable or unrelated. At the time of the study, the researcher alerted the attending doctors when a DRP was identified, so that it could be incorporated in the treatment of the patients.

For a DRP to be defined as such, it required the agreement of at least two or three members of the panel.

DRPs were individually identified and classified in seven categories as shown in Table 3.2.

Table.3. 2: DRP classification and Definitions

DRP	Operational definitions
Adverse Drug Reaction	Drug reaction due to allergy.
Drug choice problem	Contraindicated in pregnancy, renal insufficiency.
Dosing problem	Dose too low or too high to produce desired effects.
Non Compliance	Missing doses, scheduling problems or interrupting treatment prematurely.
Adverse Drug event	Toxic effects of drug.
No drug Initiation	Patient eligible for treatment but delayed initiation.

Drug–drug interactions were checked for contraindicated or not recommended combinations using national and international HIV websites (University of Liverpool HIV drug interactions website (2014); Panel on Antiretroviral Guidelines for Adults and Adolescents (2016)).

Actions or Interventions were defined as ARV Initiation, patient counseling with regard to the prescribed drug regimen, Medication changes such as ARV substitution, drug discontinuation, dosage adjustment, addition of a new drug, etc.

3.12 Data collection tools

The information for each suspected DRP was collected by the researcher from the patients' medical records and was presented in form of an individual case review. A pharmacotherapeutic team reviewed the cases and established the occurrence of a DRP, the causal relationship between the drug and subsequent problem, the rate of intervention taken to prevent a potential DRP or to resolve the actual DRP will be noted.

3.13 Data consolidation, analysis and interpretation

3.13.1 Quality evaluation

The identifiable DRPs were classified according to the Pharmaceutical Care Network Europe Version V5 (1) of 2006 (Appendix A).

In order for an event to qualify as a DRP, at least two conditions must exist:

    (i)   A patient must be likely to experience disease or symptomatology; and

    (ii)   These conditions must have an identifiable or suspected relationship with drug therapy.

3.14 Statistical Analysis

The focus was on descriptive analysis for objectives 1 and 3.

Both descriptive and inference analyses were used to answer questions of the study. For descriptive analysis, percentage or frequencies were calculated for categorical variables (Table 2). For inference statistics χ^2 was to compare the association between ARV classes and the subsequent DRP, with a cutoff of P<0.05.

The Statistical Package for Social Sciences (SPSS) version 20.0 was used for all statistical calculations.

Table 3.3: Types of variables and statistical analysis applied

Variable	Type of Variable	Descriptive analysis
Prevalence of each DRP	Categorical	Frequency or percentage
DRP (e.g., under dose, overdose, missed dose, adverse drug reactions, non-compliance, under treatment, over-treatment, drug-interactions).	Categorical	Frequency or Percentage
Rate of Intervention	Categorical	Frequency or percentage

3.15 Ethics Consideration

Permission was sought from Ndola Central Hospital Management to carry out the study at the institution. Clearance by ERES Converge IRB was sought. The research results would only be released to designated authorities. Patients willing to participate in the research were required to sign a concert form. Confidentiality was assured as no names were captured and the patient files were given codes. Medical files were not taken away from the hospital premises to avoid mix up. All information regarding the study will be kept with passwords in the Pharmacy Department and will be destroyed two (2) years after publishing the study.

CHAPTER FOUR

RESULTS

4.1 Introduction

This chapter presents the analysis and interpretation of the collected data from the research. There were 310 data collection tools that were used to collect data from the ART inpatients' Files, out of which10 were returned for incomplete data in the files. The data collection tools were in English and Bemba for easy understanding during collection.

4.2 Data analysis and interpretation

The data from the research was analyzed using SPSS 20.0 version. Descriptive and inferential statistics such as frequency tables, percentages and association or correlation tests were performed. In the data analysis, Chi square test was used to compare relationships between the variables drug related problems and ARV drug classes.

4.3 Socio-demographic characteristics of the patients

In this section the socio-demographic characteristics of study patients as respondents was presented. The socio-demographic factors considered included the name of the medical wards, Age, Gender, Current regimen and how long on current regimen.

4.3.1 Name of the medical wards

The patients' files were assessed from the 4 inpatient medical wards at Ndola Central Hospital. The results indicate that the majority 109(36.3%) of the patient files were from Male medical ward east, followed by 82(27.3%) patients from Male medical ward west, 64(21.3%) from Female medical ward west and the rest 45(15.1%) from Female medical ward east (Table 4.1).

Table.4.1: Name of medical ward where the in-patient files were studied

Name of medical ward	Frequency	Percentage (%)
Female medical ward west	64	21.3
Male medical ward west	82	27.3
Female medical ward east	45	15.1
Male medical ward east	109	36.3
Totals	300	100.00

Table.4.1 shows the names of medical ward where the in-patient files were studies.

4.3.2 Age of the in-patients studied

The Mean Age =2.70 years.

The Median Age =3.0 (40-50) years

Standard deviation=+/-0.883

The majority 127(42.3%) of the studied inpatients were between the age of 40-50 years, followed by those who were between the age of 29-39 years 91(30.3%), 55(18.3%) were above 50 years and the rest were between the age of 18-28 years 27 (9.1%) (Figure 4.1).
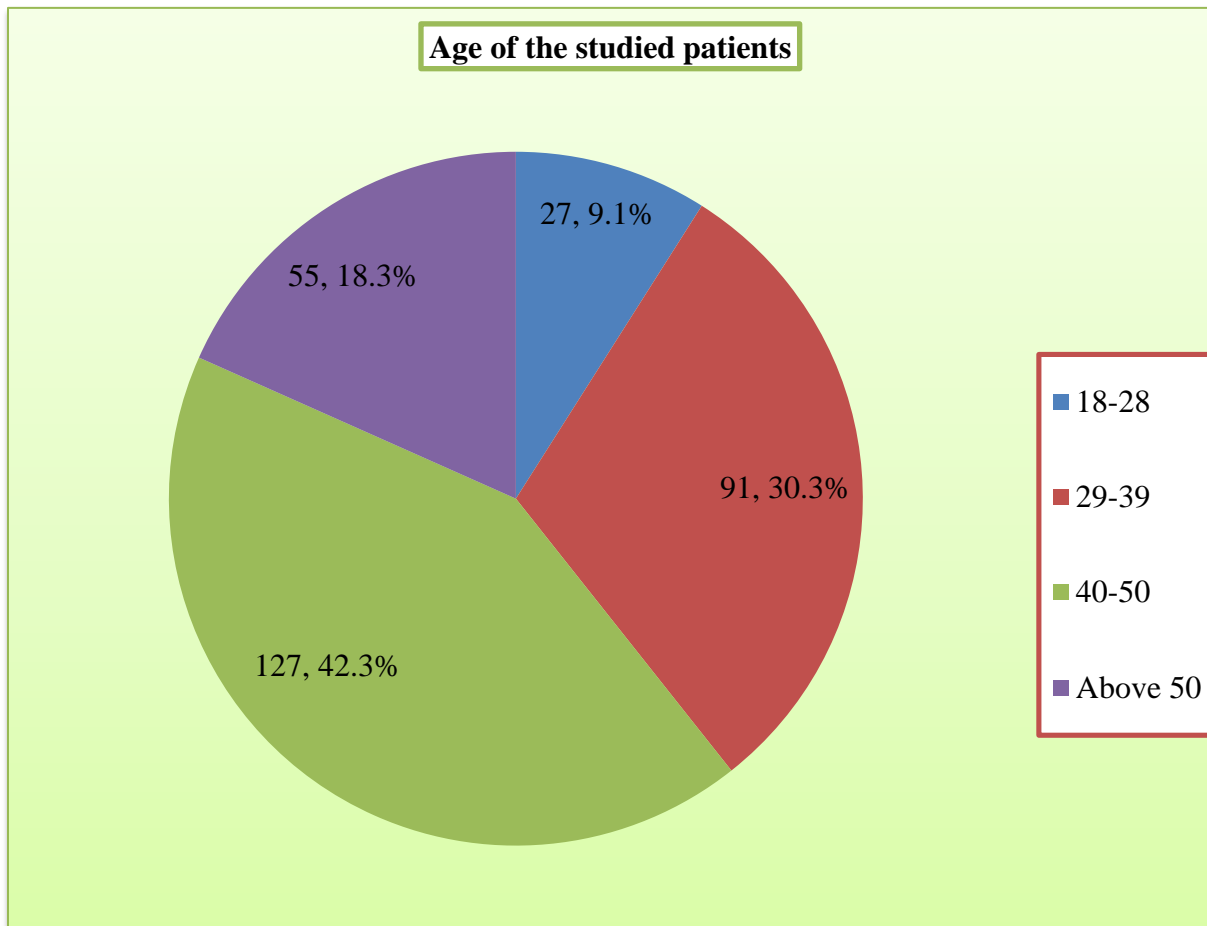
Figure.4.1: Age of the in-patients studied

The figure above shows that the majority of the patients (42.3%) studied, were aged between 40 and 50 years.

4.3.3 Gender

Out of the 300 in-patient files studied, 200 (67%) were males, while 100 (33%) were females (Figure 4.2).
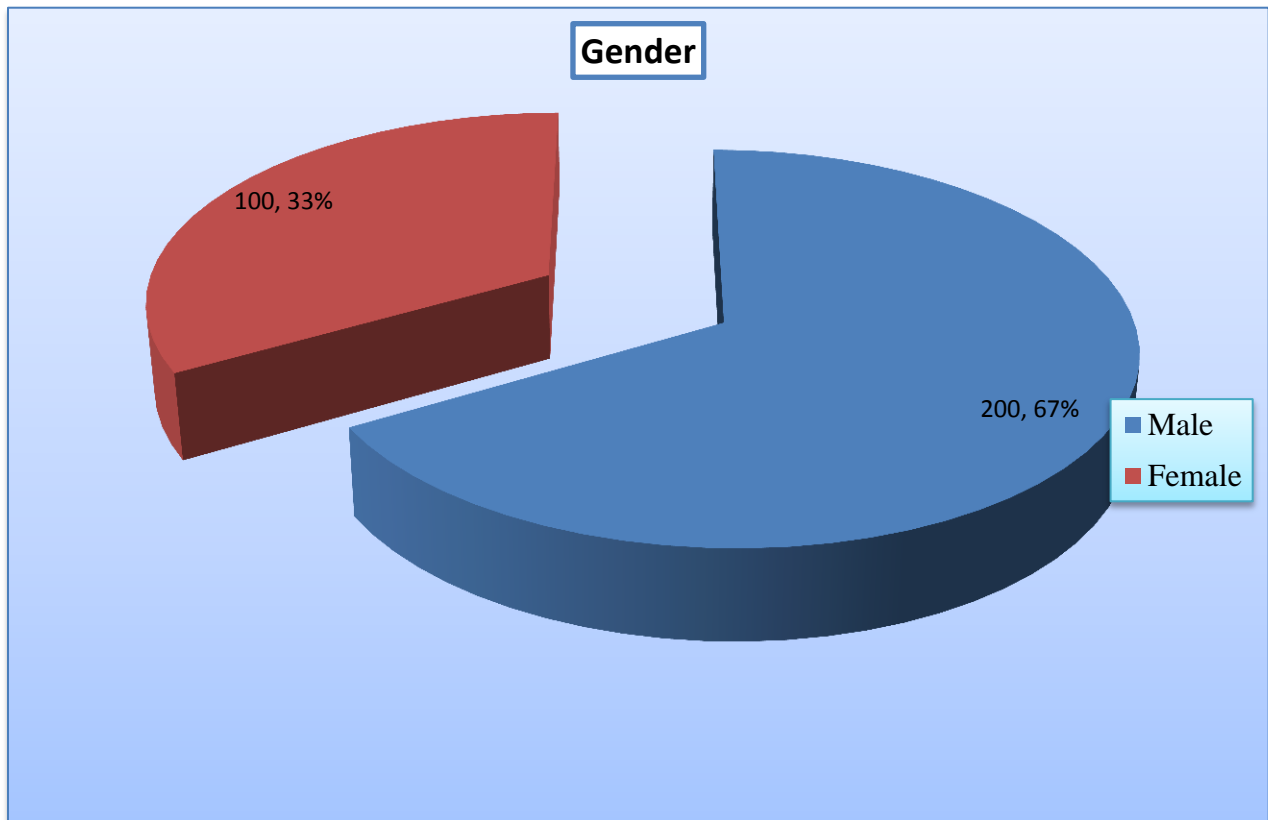
Figure.4.2: Gender of the in-patients studied
Figure 4.2 shows that the majority of the patients studied (67%), were males.

4.3.4 Current regimen

The regimen of most patients studied on was Atripla 164 (54.7%), followed by those who were not HAART 118(39.3%) and the rest 9(3%) were on ABC/3TC/LPV and Truvada/ Atazanavir respectively.

4.3.5 How long on current regimen (Period on current regimen)

Mean=**1.29 months.**

Standard deviation=+**/-0.686**

The majority were not yet on HAART or were on pre-art 146 (48.7%), followed by whose were between 1-6 months 127 (42.3%), above 12 months 18 (6%) while the rest were between 7-12 months 9 (3%) on the current regimen (Table 4.2).

Table.4.2: ART Regimens and Duration of ART treatment studied

ART Regimen	Number of patients	Percent (%)
Atripla	164	54.7
ABC/LPV	9	3.0
Truvada/Atazanavir	9	3.0
Not on HAART	118	39.3
Totals	300	100.00
Duration of ART Treatment		
1-6 months	127	42.3
7-12 months	9	3.0
Above 12 months	18	6.0
Not on HAART	146	48.7
Totals	300	100.00

Table 4.2 shows the number of patients on ART Regimens and duration of ART treatment of the patients studied.

4.4. Prevalence of Drug Related Problem associated with ARVs.

The overall prevalence of drug related problem associated with ARVs was at 94 (31.25%). This represents a high prevalence of drug related problems associated with ARVs (Figure 4.3). The result of this study is similar to the results of studies done by Commers *et al* (2013) that documented a prevalence of 35.1% for the identified DRPs and Yehia *et al* (2012) that recorded a prevalence of 29% on their first day of the study.

Prevalence of DRP associated with ARVs

94, 31%

206, 69%

■ Yes
■ No
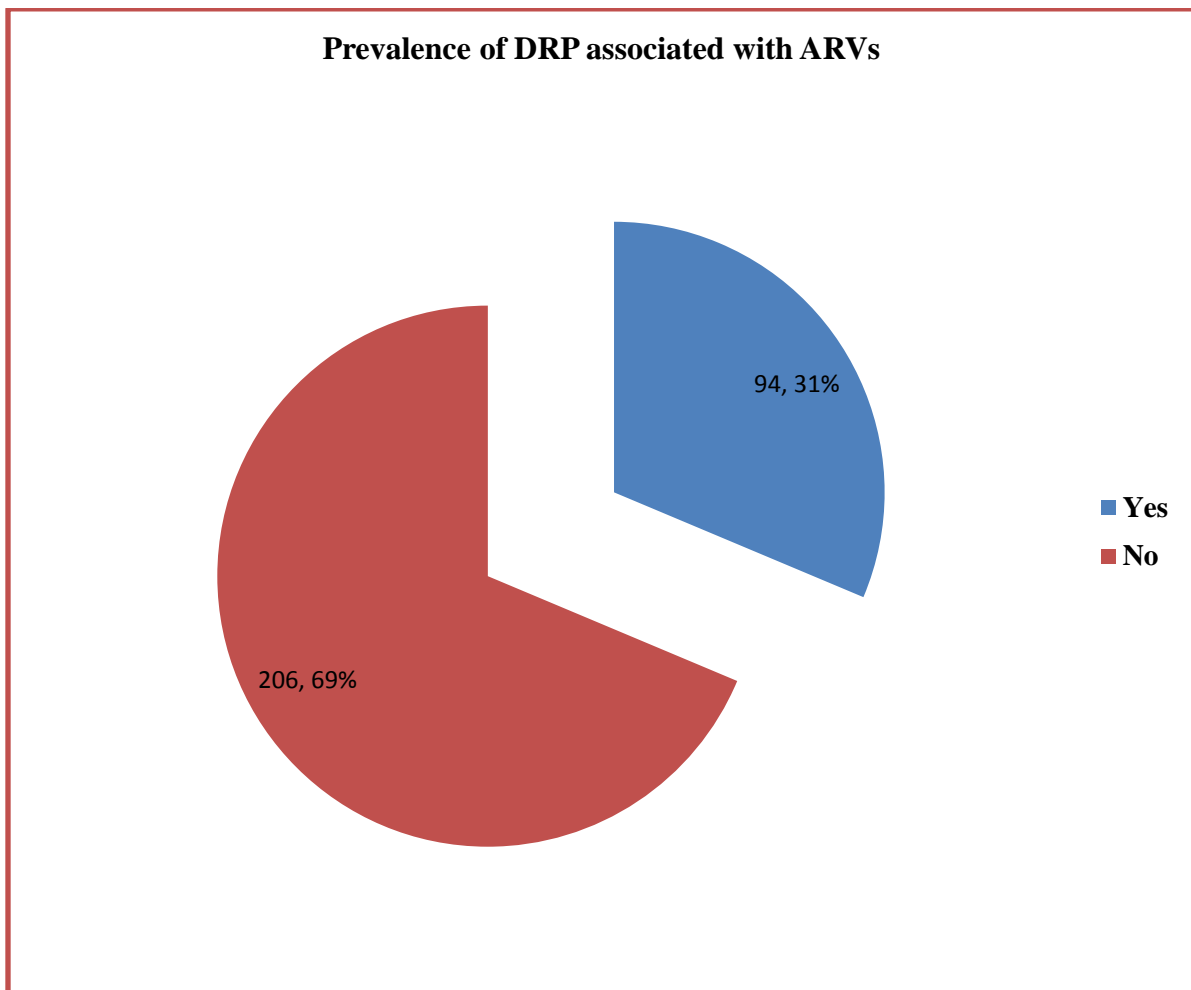
Figure .4.3: Prevalence of DRP associated with ARVs

Figure 4.3 shows the Prevalence of Drug Related Problems associated with ARVs at 31 %.

4.4.1 Category of the presence of a drug related problem associated with ARVs

Out of 300 inpatient files studied, the majority 204 (68%) had no drug related problem associated with ARVs, followed by 22 (66%) who had definitely a presence of Drug related problem, while the rest 10 (30%) had a possibly the presence of a drug related problem Figure 4.4).
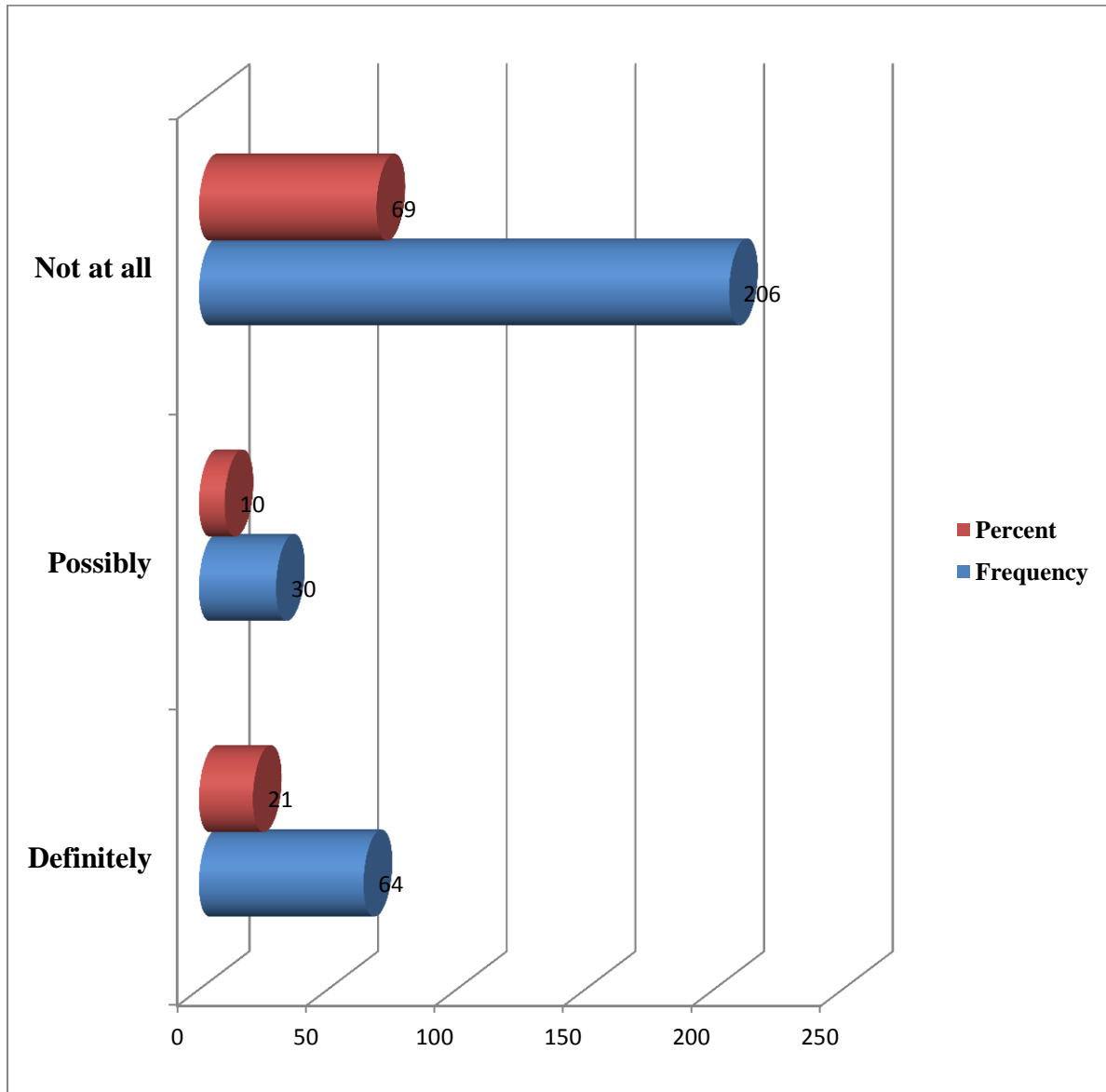
Figure.4.4: Category of the presence of a drug related problem associated with ARVs

Figure.4 shows the category of the presence of a drug related problem associated with ARVs.

4.5 prevalence of each Drug related problem associated with ARVs.

The common type of drug related problems associated with ARVs were adverse drug event 38 (40%), non-compliance representing 38 (40%) and no drug initiation 18 (20%) (Figure.4.5).
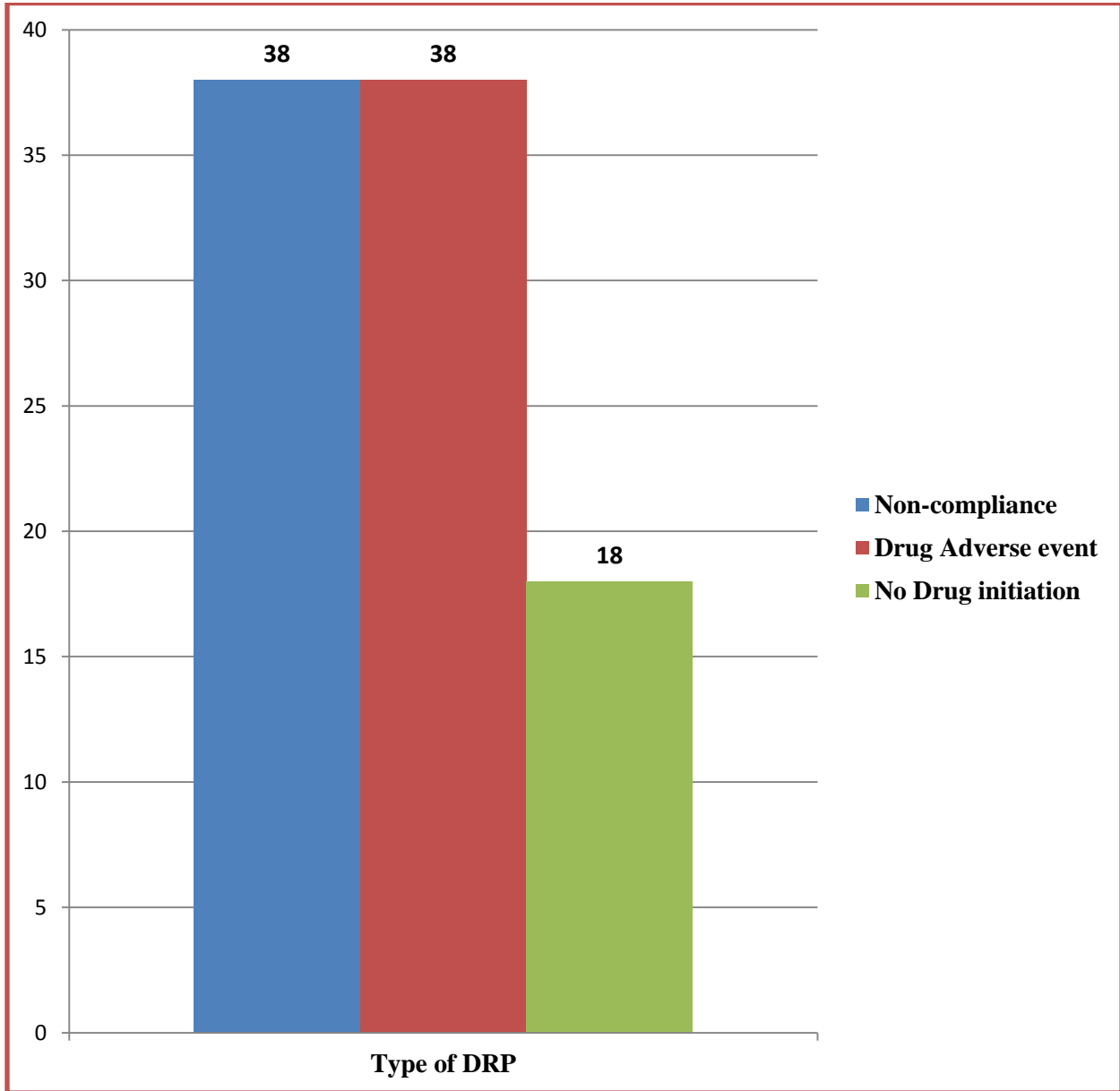
Figure.4.5: Prevalence of each Drug related problems associated with ARVs

Figure.4.5 shows the Prevalence of each Drug related problems associated with ARVs.

4.5.1 Classes of ARVs associated with drug related problem in HIV/AIDS patient

The classes of ARVs associated with drug related problems in the management of HIV/AIDS patients was Non-Nucleoside Reverse Transcriptase inhibitors representing 47 (50%) patients, followed by Nucleoside Reverse Transcriptase inhibitors and Protease inhibitors representing 42(45%) and 5(5%) patients respectively (Figure.4.6).
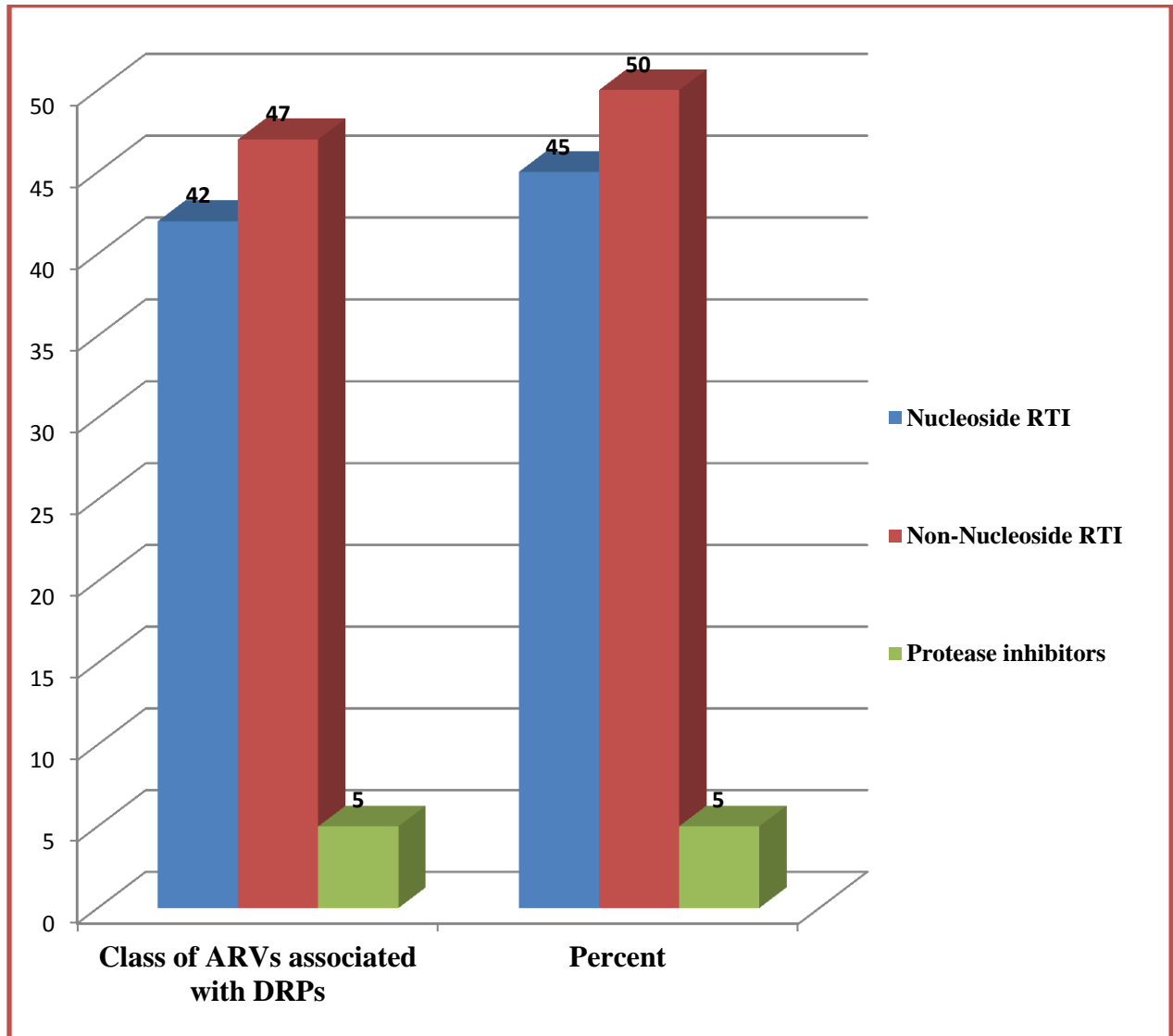
Figure.4.6: Classes of ARVs associated with drug related problem in HIV/AIDS patient

The figure above shows that Non-Nucleoside RTIs was most associated with drug related problems.

4.6 Antiretroviral drug classes associated with drug related problems in HIV/AIDS patients.

4.6.1 Chi-Square test statistic $(\chi)^2$

The Chi-square test examines the relationship between two variables at nominal and discrete level in quantitative or qualitative research. The Chi-square test offers an alternate method of testing the significance of difference between two proportions. It has the advantage in that; it can also be used when more than two groups are being compared. The test compares the actual frequencies with the expected outcomes or how close they match or differ from the expected distribution and whether two variables are independent or not. In this study if the p-value is less than 0.05 (*p<0.05*) significance level, then there is a significant association between the variables drug related problem and ARV drug class, while if the p-value is greater than 0.05 (*p>0.05*) significance level, then there is no association between the variables. (Park K, 2011 p.789). Chi square and cross tabulation was used to answer the above question and the results were as shown in table 4.6 below.

Table.4.3: Relation between ARV drug classes and Drug Related problems using Pearson chi square.

Class of ARVs	DRP	P value
NRTIs	Adverse Drug Event	0.03^{*}
NRTIs	Non-compliance	0.011^{*}
NRTIs	No drug initiation	$0.982^{\#}$
NNRTIs	Adverse Drug Event	$0.674^{\#}$
NNRTIs	Non-compliance	$0.401^{\#}$
NNRTIs	No drug initiation	$0.294^{\#}$
PIs	Adverse Drug Event	$0.984^{\#}$
PIs	Non-compliance	$0.339^{\#}$
PIs	No drug initiation	$0.223^{\#}$

Table 4.3 shows the relation between the ARV drug classes and Drug related problems using Pearson chi square.

* P value is< 0.05 significant level. Therefore, there is a significant association between NRTIs and Adverse drug event and between NRTIs and Non-compliance.

P value is > 0.05 significant level. Therefore, there is no significant association between ARV drug classes and Drug Related problems.

4.7 The rate of interventions to prevent or resolved Drug related problems associated with HIV/AIDS patients.

Out of 94 patients that experienced DRPs, 23 (24%) patients experienced interventions to prevent or resolve drug related problems associated with HIV/AIDS patient while 71 (76%) had No intervention to prevent or resolve a drug related problem. This result indicates that there was a low rate of interventions to prevent or resolve drug related problems associated with HIV/AIDS patients (Figure 4.7). This result is similar to that of Abah *et al* (2014) that documented a 0.9% intervention rate towards DRPs.

The rate of intervention involved to prevent or resolve DRP

23, 24%   71, 76%   71, 76%   ■ Yes ■ No
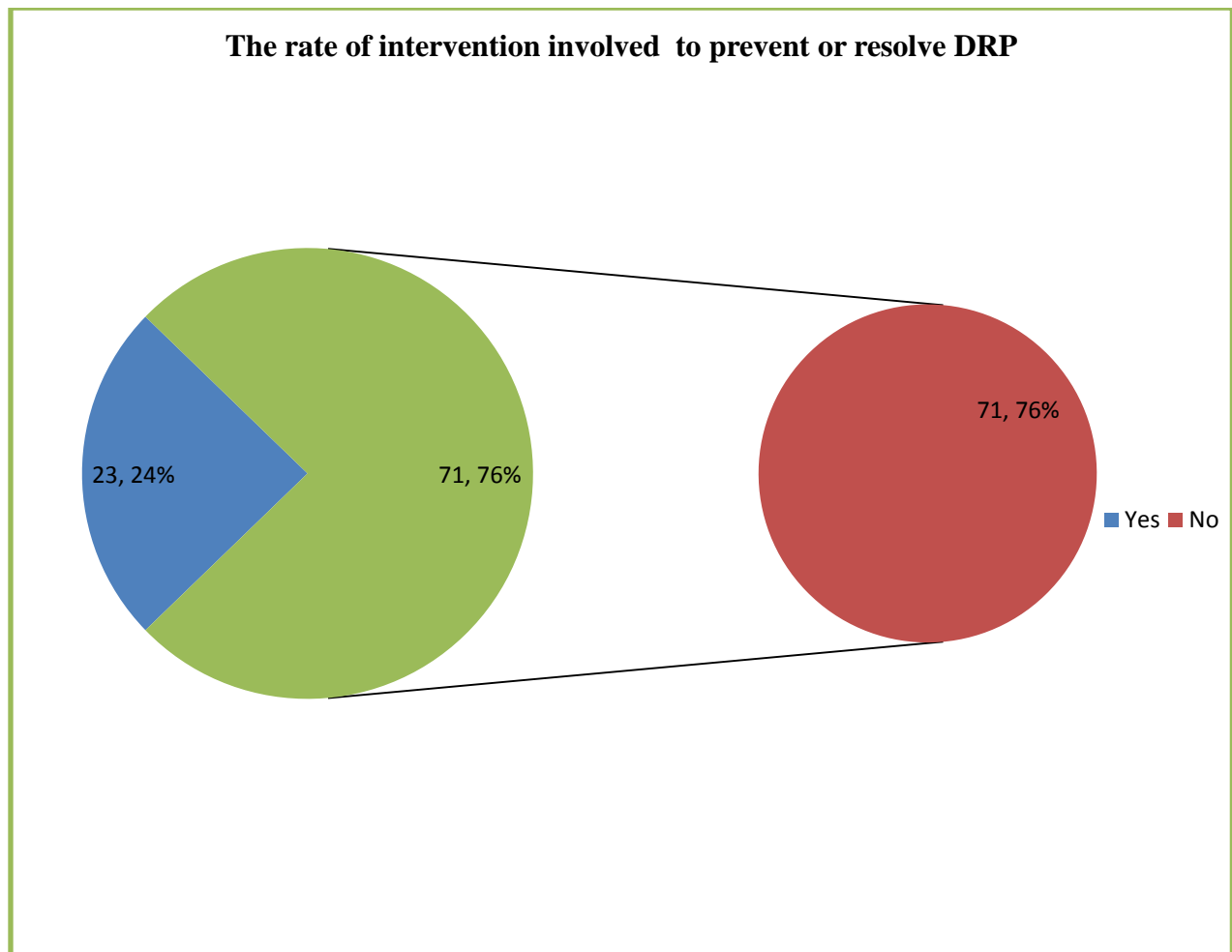
Figure.4.7: Rate of interventions to prevent or resolve drug related problems associated with HIV/AIDS patients.

This figure shows that the rate of intervention was 24%.

4.7.1 Type of drug intervention involved to prevent or resolve DRP

The interventions involved in preventing or resolving drug related problems in HIV/AIDS patients were change of drug 11 (48%), followed by Adherence counseling 8 (36%) and stopping of drug 4 (16%) (Figure 4.8).
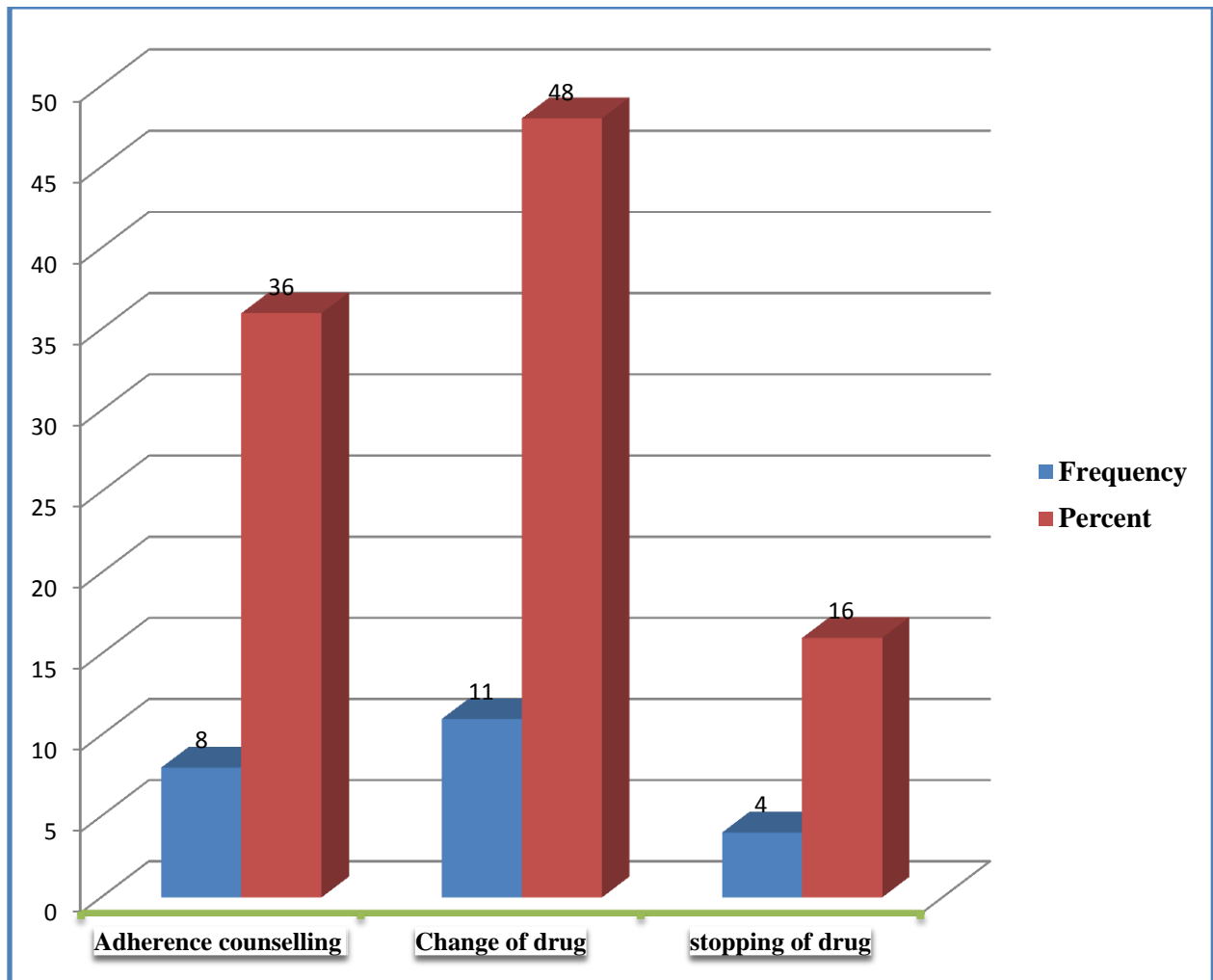
Figure.4.8: Interventions involved in preventing or resolving drug related problems in HIV/AIDS patients.

The figure above shows that most of the interventions involved were change of drug (48%).

Table 4.4 Types of Intervention in each DRP

DRP	Adherence counseling	Change of drug	Stopping of drug	Initiation of ARV	No intervention
Non Compliance	4	6	0	0	35
Adverse drug event	4	5	4	0	11
No drug initiation	0	0	0	0	23
Total	8	11	4	0	69

Table 4.4 shows that 11 (48%) patients had their drugs changed due to DRPs.

CHAPTER FIVE

DISCUSSION

The results of this study indicate that the prevalence of Antiretroviral DRPs is high (31%). The finding of 31% ARV DRPs falls within the range of 25.8% to 72% prevalence of ART administration DRPs in an inpatient setting for patients on ART in studies done by Synder *et al*, (2011); Yehia *et al*, (2012); Merchen *et al,* (2011). The result of this study is similar to the results of studies done by Commers *et al* (2013) that documented a prevalence of 35.1% for the identified DRPs and Yehia *et al* (2012) that recorded a prevalence of 29% on their first day of the study. The result of this study, however, is higher than the result of a study by Carcelero *et al,* (2011), that found the prevalence of Antiretroviral related problems to be 21.7%. The high prevalence of DRPs in this study is a concern, given DRPs severely compromise effectiveness of drug therapy and is linked with the likelihood of drug resistance. Drug related problems are unacceptable, regardless of disease state, and the goal for all institutions should be no DRPs. The high prevalence of drug related problems in this study could be due to lack of provider experience in HIV related services, the failure to indicate in the patient's chart and/or Files the antiretroviral drugs that the patient is taking and lack of clinical pharmacists on the ward round to review medication orders. Synder *et al* (2011), interviewed providers who had committed medication errors (DRPs), in an attempt to discover the underlying causes of these errors, found that most errors were due to lack of expertise with prescribing ARVs, failure to reconcile home/transfer medications, poor or no written/verbal communication between providers, overlooking decision support software alerts and/or lack of ownership for HIV therapy when treating patients. Merchen *et al* (2011) further demonstrated that review by a pharmacist with HIV expertise reduced errors and was cost-effective. They suggested the implementation of a review of all ART by a specialized HIV pharmacist to avoid unnecessary harm and expense (Merchen *et al*, 2011). Heelon *et al*. agreed with the efficacy of this strategy. These authors in agreement investigated the duration of inpatient ART medication errors with and without the intervention of an HIV clinical pharmacist, and found that the intervention of an HIV pharmacist decreased the time to error correction from 84 h to 15.5 h. In order to overcome such obstacles to treatment, it would be beneficial for institutions to provide education and resources regarding

ART, utilize Clinical Pharmacists review of Medication orders and encourage consultation from infectious diseases practitioners when complicated HIV patients are admitted to the hospital.

The prevalence of each Drug related problem associated with anti-retroviral drugs in the management of HIV/AIDS patients were adverse drug event (40%), noncompliance (40%) and no drug initiation (20%) (Figure 4.5). The result of this study differs from several similar studies that documented the prevalence of each drug related problem associated with ARVs in the management of HIV/AIDS patients. Ojeh *et al* (2015) shows that the most common type of DRPs was a drug omission (21.7%), followed by unnecessary drug (13.1%) and wrong drug indication(13.1%) respectively. Abah *et al* (2014) documented the most common type of DRP as an untreated indication (49.3%), followed by therapeutic failure (25.9%) and drug toxicity (22.9%). Carcelero *et al* (2011) in Spain, observed that the most common DRP was contraindicated combinations (drug-drug interactions) at 33.3%, followed by incorrect dose (low or high) at 16%, and dose omission at 15%. Molinio *et al* (2014) identified adverse drug reactions as the most prevalent DRPs. Failure to initiate ART to eligible patients in this study is one DRP which is worth noting. This scenario could have been due to the presence of opportunistic infections like Tuberculosis (TB), where the attending physician first decides to treat the OI and delay ART for fear of ART inducing Immune Reconstitution Inflammatory Syndrome. Prompt initiation of ART has profound patient and population level benefits, because the use of ART not only reduces HIV and non HIV related morbidity and mortality among HIV-infected patients, most significant among those with a lower CD4 count, but also significantly reduces the rate of HIV transmission to currently uninfected persons (WHO, 2013). The START and TEMPRANO studies that were conducted in Cote DI Ivore are two large randomized studies which showed that early initiation of ART reduced active TB, particularly in countries with a high prevalence of HIV/TB co-infection (Panel on Antiretroviral Guidelines for Adults and Adolescents (2016). To highlight the importance of early initiation of ART, national and international guidelines have continued to evolve and the Zambia Consolidated Guidelines (2014) and the Panel on Antiretroviral Guidelines for Adults and Adolescents (2016) now recommend ART initiation for individuals with HIV, regardless of the CD4 count levels, whereas the WHO (2013) recommends the initiation of ART in HIV positive adults with a CD4≤500 cells/mm^3. The variation in the prevalence of DRPs between studies could be due to

the following reasons: (i) the definition and methods used to identify the DRPs; (ii) the heterogeneous estimates of the reported prevalence, and (iii) the risk factors associated with these DRPs. The patterns and severity of DRPs may differ because of local environmental and genetic influences. The mode of data extraction to identify DRPs can also affect the patterns of drug related problems in that prescriptions may not capture patient characteristics such compliance to ARV medication, CD4 count to determine eligibility to initiate ART, patients renal function status to determine the correct ARV or the dose of ARV to give. In summary, the differences in the patterns of DRPs in the various studies are due to the fact that the causes of DRPs are multi factorial (Champias et al, 2014).

In this study, we have shown that only the ARV class Nucleoside Reverse Transcriptase Inhibitor (NRTI) is significantly associated with adverse drug events and Non Compliance, in the management of patients with HIV/AIDS (Table 4.4). The finding of this study is similar to a study done by Commers *et al* (2013) which found that NRTIs were associated with a high risk of prescribing error (DRP) but differs with Champias *et al* (2015), who found no statistical association between a specific ARV or ARV class and a specific DRP. The fact that NRTIs are often the 'backbone' of the cART makes them the most frequently prescribed class of ARVs, hence, increases the risk of DRPs. A study done in Kenya by Arika (2011) demonstrated that parents that were on ART was significantly associated with adherence (noncompliance) and further determined a statistically significant association between caregivers difficulty in adhering to own ARV medication and child's adherence/non-adherence outcome with a p<0.05.

Our results indicate that 24% was the rate of intervention to prevent or resolve drug related problems associated with HIV/AIDS patients (Figure 4.6). This intervention rate is low and is comparable to a study done by Abah *et al* (2014) that documented a 0.9% intervention rate of the population seen during the study period. However, this result is lower than that documented by other studies done by Agu *et al* (2014) that documented that 98.3% of participants who had medication errors (DRPs) received interventions for the medication errors and 97.4% of the potential/actual DRPs were resolved. Chiampas *et al* (2015) observed that documented correction of DRPs for the clinical specialist was approximately 50%. Carcelero *et al* (2011) documented a 100% intervention in all the 60 DRPs detected.

The low rate of intervention in our study could be attributed to underreporting of the interventions in DRPs. Under reporting of interventions by Pharmacist/or physicians is a well-known phenomenon observed in other studies (Boardman *et al*, 2001; Yehia *et al,* 2012; Abah *et al,* 2014). Boardman *et al* (2001) analyzed pharmacist's activities on the ward and discovered that under one-third (31%) of interventions were actually recorded. The interventions that were documented tended to be those of highest clinical importance and those that were time consuming to the pharmacist. Boardman *et al* (2001) further explained that lack of time was the major reason interventions were not documented. Under-reporting of interventions may have been due to lack of a pharmacist (Clinical or not) during ward rounds to conduct and document interventions on DRPs. Scott *et al* (2010) showed that HIV pharmacist led interventions such as ARV regimen simplifications and adherence counseling were associated with better therapy outcomes, with 98% of patients able to accomplish or maintain undetectable viral loads post intervention compared with 63% pre intervention. Abah *et al* (2014), in agreement, observed a favorable HIV virological and immunological outcomes post pharmacist intervention by showing that among patients whom virological failure was documented 81% achieved viral suppression post intervention.

5.1 Limitations

The following limitations to the study were identified:
- A limitation of our study is that there were no HIV clinical specialists (Pharmacists and physicians) with training in HIV pharmacotherapy to play an important role in correcting DRPs.
- The small sample size, which limits the identification of other drug related problems associated with ARVs, other than the ones that were documented (e.g., adverse drug reactions, drug interactions) that might also have been experienced by HIV/AIDs patients.
- The study only covered the department of Internal Medicine of the institution and only in patients had their records reviewed.
- The study only involved review of patients' records.

CHAPTER SIX

CONCLUSION AND RECOMMENDATIONS

6.1 Introduction

This chapter includes a summary of the key findings based on the objectives of this study and evaluation of the study in terms of the rate of intervention to prevent or resolve drug related problems associated with ARVs in the management of HIV/AIDs patients at the Ndola central Hospital.

6.2 Conclusion

The study revealed a high prevalence of DRPs with a risk of DRPs being high in patients taking NRTIs. The Antiretroviral drug related problems identified in the study were Adverse drug event, Noncompliance and No Antiretroviral drug initiation.
There was a low rate intervention in these DRPs which can lead to the development of ARV resistance and treatment failure over time.

6.3 Recommendations

1. There need to train HIV clinical specialists (Pharmacists and physicians) in HIV pharmacotherapy that can play an important role in identifying and correcting DRPs associated with ARVs in the management of HIV/AIDs patients.
2. There is need to incorporate the identification and prevention/resolution of drug related problems associated with ARVs in the treatment guidelines for HIV/AIDs.
3. There is a need to strengthen or develop strategies that will encourage HIV/AIDs patients accept their sero-positive status and hence encourage compliance to the prescribed ARV regimens.
4. There is a need for further studies to be conducted that will look at factors that increase the risk of drug related problems associated with ARVs such as local environmental and genetic factors.

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APPENDICES

Appendix A: PCNE Classification V5.01

Primary domain	Code V5.01	Problem
1. Adverse Reactions **P**atient suffers from an adverse drug event	**P1.1** **P1.2** **P1.3**	**Side effect suffered (non-allergic)** **Side effect suffered (allergic)** **Toxic effects suffered**
2. Drug choice Problem patient gets or is going to get a wrong (or no drug) drug for his/her disease and/or condition	P2.1 P2.2 P2.3 P2.4 P2.5 P2.6	Inappropriate drug (not most appropriate for indication) Inappropriate drug form (not most appropriate for indication) Inappropriate duplication of therapeutic group or active ingredient Contra-indication for drug(including Pregnancy/breastfeeding) No clear indication for drug use No drug prescribed but clear indication
3. **Dosing problem** Patient gets more or less than the amount of drug he/she requires	p3.1 P3.2	drug dose too low or dosage regime not frequent enough Drug dose too high or dosage regime too frequent Duration of treatment too

	P3.3	short
	P3.4	Duration of treatment too long.
4. Drug use problem Wrong or no drug taken/administered	**P4.1** P4.2	drug not taken/administered at all Wrong drug taken/administered
5. Interactions there is a manifest or potential drug-drug or drug-food interaction	P5.1 P5.2	potential interaction Manifest interaction
6. others	P6.1 P6.2 P6.3 P6.4	Patient dissatisfied with therapy despite taking drugs correctly Insufficient awareness of health and diseases(possibly leading to future problems) Unclear complaints. Further clarification necessary Therapy failure(reason unknown)

Appendix B: Participant Information Sheet (To be kept by the participant)

Research Title: Drug related problems in the management of HIV/AIDs patients at Ndola Central Hospital.

Dear Participant,

We have invited you to participate in a study which is designed to provide information on the prevalence and patterns of Drug related problems in the management of HIV/AIDs patients at Ndola Central Hospital in 2016.

In order to intervene (i.e., prevent or resolve) in a patient's drug therapy prospectively and consistently, and to document how that intervention can lead to positive outcomes, it is important to identify and understand the different types of patient-specific **Drug Related Problems** that a patient might develop.

If you are willing to participate in this study, we shall go through your clinical records (medical notes, drug charts).

What are we asking you to do?

During the study we will only ask for your permission to go through your clinical records.

Confidentiality

Any information obtained will remain absolutely confidential. Your details will be entered on a paper form but only in coded form and your name will not be included. Only your enrolment number will be recorded.

The Study is voluntary

You do not have to participate in the study if you do not want to, and if you refuse to participate in the study, your care will not be affected in any way. If you agree, you are also free to change your mind at a later date.

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Consent Form (To be kept by the researcher)

I confirm that I have understood the information I have been given about the study. I agree to participate in the study. I confirm that I am joining the study out of my free will and that I can withdraw at any time without affecting the quality of care available to me.

I understand what will be required of me.

Name:

Date:

Sign:

I confirm that I have explained the information fully and answered questions.

Name of researcher:

Signed:

Date:

IFIFWILE UKWISHIBIKWA KULI ABO ABALEFWAIKA MULI IYI IMILIMO

Umutwe waiyi imilimo: amafya yasangwa mukunwa umuti wabulwele bwa kashishi ka HIV/AIDS.

Kubalesangwamuliiyimilimo,

Tulemilomba ukuba muli iyi milimo yakusanga amafya yasangwa mukunwa umuti wabulwele bwakashishika HIV/AIDS pano pachipatala cha Ndola Central Hospital uno mwakawa 2016.

Pakuti abalwele babe abayafwilishiwa ilyo amafya yacili yalechiti kano kuti fyonse ifyaliombwa, chaliba icikankala ukwishiba imisango yapusana pusana iya mafia ayasangwa mukundapwa kuli ububulwele yeshilamo.

Ngamuli aba kukukaukuba muli iyi milimo, tukalomba ukubomfya ifitabo fyamiti yenu muno mu chipatala.

Finshi tulemilomba ukucita?

Muli iyi milimo yesu, tukalalomba ulusa pakubonfyako ifitabo fyamiti yenu muno mu chipatala.

Inkama

Tulelaya inkama yafyonse ifyo tukalafunya mu fitabo fyamiti.Neshina lyenu tatwakalalemba, lelo, tukalembafye icipendo chaimwe mwe basuminishi waukuba muli iyi milimo.

Imilimo iyi yakuipelesha

Ukusangwa muli iyi milimo cili chakakuipelesha. Ngatamulefwaya, tamufwileukusangwamo, lelo ngamwasuminisha ukubamo, muli abakakulwa ukuleka ilyo lyonse mwafwaya.

Abakutumina nga mulefwaya ifilifyonse pali iyi milimo:

Ishina: KalaleMunenu(Master of Clinical Pharmacy Student)

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     +260 955 155 633

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ICHISUMINIISHO

Ndesumina ukuti muli iyi imilimo yakwafwilisha amafya ayasangwa mukunwa umuti wabulwele bwakashishi ka HIV. Ndesumina ukuti tabalempatikisha iyo ukuba umu muli abo abali muli iyi imilimo. Kabili nabalondolola ukuti ndi uwasuminishiwa ukuleka panshita ningafwailapo nemwine ukwabula ukufulunganya ukundapwa kwandi pano pa chipatala.

Ningumfwa nokwishiba ifilefwaika ine ukuchita.

Ishina lyandi:

Pa bushiku:

Ukusaina:

Nasumina ukuti nalondolola fyonse namepusho ninjasuka.

Ishina lyandi:

Pa bushiku:

Ukusaina:

Appendix C: Data Collection Tool

TITLE: DRUG RELATED PROBLEMS ASSOCIATED WITH ANTI RETROVIRAL THERAPY OF HIV/AIDS PATIENTS AT NDOLA CENTRAL HOSPITAL

Ward: ………………….

Patient code: ……….

Age: ……………………..

Gender: ………………..

Diagnosis: ……………

Symptoms:

…………………………………………………………………………………………

…………………………………………………………………………………………

………………………………………………………………………………

Current Regimen……………………………………………………………….....

How Long on current regimen:..

How long on ART: ……………………………………………………………………

Drug   History:

....

....

Complaints:

....

....

Data Collection Tool

Presence of Drug Related Problem	Definitely possibly not at all
Type of Drug Related Problem	
Drug Associated with Drug Related Problem	
Intervention involved	

Appendix D: SPSS Extracts

1. SOCIO-DEMOGRAPHIC CHARACTERISTICS
The mean and Standard Deviation [Age and How long on the current Regimen]

Statistics

		Age of patient	How long on the current Regimen
N	Valid	300	300
	Missing	2	2
Mean		2.70	2.61
Std. Deviation		.871	1.437

Name of the medical ward

Name of ward

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Female medical ward west	64	21.2	21.3	21.3
	Male medical ward west	82	27.2	27.3	48.7
	Female medical ward east	45	14.9	15.0	63.7
	Male medical ward east	109	36.1	36.3	100.0
	Total	300	99.3	100.0	
Missing	System	2	.7		
Total		302	100.0		

Age of patients

Age of patient

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	18-28	27	8.9	9.0	9.0
	29-39	91	30.1	30.3	39.3
	40-50	127	42.1	42.3	81.7
	Above 50	55	18.2	18.3	100.0
	Total	300	99.3	100.0	
Missing	System	2	.7		
Total		302	100.0		

Gender of patient

Gender of patient

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	200	66.2	66.7	66.7
	Female	100	33.1	33.3	100.0
	Total	300	99.3	100.0	
Missing	System	2	.7		
Total		302	100.0		

ART regimen of the patient

Current Regimen

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	ATRIPLA	164	54.3	54.7	54.7
	ABC/3TC/LPV	9	3.0	3.0	57.7
	Truvada/alazanavir	9	3.0	3.0	60.7
	Not on HAART	118	39.1	39.3	100.0
	Total	300	99.3	100.0	
Missing	System	2	.7		
Total		302	100.0		

Duration of ART treatment

How long on the current Regimen

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1-6 Months	127	42.1	42.3	42.3
	7-12 months	9	3.0	3.0	45.3
	Above 12months	18	6.0	6.0	51.3
	Not on HAART	146	48.3	48.7	100.0
	Total	300	99.3	100.0	
Missing	System	2	.7		
Total		302	100.0		

2. PREVALENCE OF DRUG RELATED PROBLEM ASSOCIATED WITH ARVS.

Presence of drug related problem

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	94	31.1	31.3	31.3
	No	206	68.2	68.7	100.0
	Total	300	99.3	100.0	
Missing	System	2	.7		
Total		302	100.0		

Category of the presence of a drug related problem associated with ARVs

Categatory of Presence of drug related problem

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Definitely	64	21.2	21.3	21.3
	Possibly	30	9.9	10.0	31.3
	Not at all	206	68.2	68.7	100.0
	Total	300	99.3	100.0	
Missing	System	2	.7		
Total		302	100.0		

3. DRUG RELATED PROBLEMS ASSOCIATED WITH ARVS.

Is non-compliance the type of DRP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	38	12.6	40.4	40.4
	No	56	18.5	59.6	100.0
	Total	94	31.1	100.0	
Missing	System	208	68.9		
Total		302	100.0		

Is Adverse drug event the type of DRP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	38	12.6	40.4	40.4
	No	56	18.5	59.6	100.0
	Total	94	31.1	100.0	
Missing	System	208	68.9		
Total		302	100.0		

Is no drug initiation the type of DRP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	18	6.0	19.1	19.1
	No	76	25.2	80.9	100.0
	Total	94	31.1	100.0	
Missing	System	208	68.9		
Total		302	100.0		

4. CLASSES OF ARVS ASSOCIATED WITH DRUG RELATED PROBLEM IN HIV/AIDS PATIENT

Is Nucleoside RTI a class of ARV associated with DRP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	42	13.9	44.7	44.7
	No	52	17.2	55.3	100.0
	Total	94	31.1	100.0	
Missing	System	208	68.9		
Total		302	100.0		

Is Non- Nucleoside RTI a class of ARV associated with DRP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	47	15.6	50.0	50.0
	No	47	15.6	50.0	100.0
	Total	94	31.1	100.0	
Missing	System	208	68.9		
Total		302	100.0		

Is Protease inhibitors a class of ARV associated with DRP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	5	1.7	5.3	5.3
	No	89	29.5	94.7	100.0
	Total	94	31.1	100.0	
Missing	System	208	68.9		
Total		302	100.0		

5. ASSOCIATION BETWEEN ANTI RETROVIRAL DRUG CLASSES AND DRUG RELATED PROBLEMS IN HIV/AIDS PATIENTS.

Relationship between Nucleoside Reverse Transcriptase inhibitors and adverse drug event

Is Nucleoside RTI a class of ARV associated with DRP * Is Adverse drug event the type of DRP Cross tabulation

		Is Adverse drug event the type of DRP		
		Yes	No	Total
Is Nucleoside RTI a class of ARV associated with DRP	Yes	24	18	42
	No	14	38	52
Total		38	56	94

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	8.810[a]	1	.003		
Continuity Correction[b]	7.600	1	.006		
Likelihood Ratio	8.900	1	.003		
Fisher's Exact Test				.004	.003
Linear-by-Linear Association	8.717	1	.003		
N of Valid Cases[b]	94				

Relationship between Nucleoside Reverse Transcriptase inhibitors and Non- compliance

Is Nucleoside RTI a class of ARV associated with DRP * Is non-compliance the type of DRP Cross tabulation

		Is non-compliance the type of DRP		
		Yes	No	Total
Is Nucleoside RTI a class of ARV associated with DRP	Yes	11	31	42
	No	27	25	52
Total		38	56	94

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	6.388[a]	1	.011		
Continuity Correction[b]	5.364	1	.021		
Likelihood Ratio	6.530	1	.011		
Fisher's Exact Test				.019	.010
Linear-by-Linear Association	6.320	1	.012		
N of Valid Cases[b]	94				

Relationship between Nucleoside Reverse Transcriptase inhibitors and No drug initiation

Is Nucleoside RTI a class of ARV associated with DRP * Is no drug initiation the type of DRP Cross tabulation

		Is no drug initiation the type of DRP		
		Yes	No	Total
Is Nucleoside RTI a class of ARV associated with DRP	Yes	8	34	42
	No	10	42	52
Total		18	76	94

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.001[a]	1	.982		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.001	1	.982		
Fisher's Exact Test				1.000	.597
Linear-by-Linear Association	.000	1	.982		
N of Valid Cases[b]	94				

Relationship between Non-Nucleoside reverse transcriptase inhibitors and adverse drug event

Crosstab

		Is Adverse drug event the type of DRP		
		Yes	No	Total
Is Non- Nucleoside RTI a class of ARV associated with DRP	Yes	18	29	47
	No	20	27	47
Total		38	56	94

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.177[a]	1	.674		
Continuity Correction[b]	.044	1	.834		
Likelihood Ratio	.177	1	.674		
Fisher's Exact Test				.834	.417
Linear-by-Linear Association	.175	1	.676		
N of Valid Cases[b]	94				

Relationship between Non-Nucleoside reverse transcriptase inhibitors and Non compliance

Crosstab

		Is non-compliance the type of DRP		
		Yes	No	Total
Is Non- Nucleoside RTI a class of ARV associated with DRP	Yes	17	30	47
	No	21	26	47
Total		38	56	94

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.707[a]	1	.401		
Continuity Correction[b]	.398	1	.528		
Likelihood Ratio	.708	1	.400		
Fisher's Exact Test				.529	.264
Linear-by-Linear Association	.699	1	.403		
N of Valid Cases[b]	94				

Relationship between Non-Nucleoside reverse transcriptase inhibitors and No drug initiation

Crosstab

		Is no drug initiation the type of DRP		
		Yes	No	Total
Is Non- Nucleoside RTI a class of ARV associated with DRP	Yes	7	40	47
	No	11	36	47
Total		18	76	94

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1.099[a]	1	.294		
Continuity Correction[b]	.618	1	.432		
Likelihood Ratio	1.107	1	.293		
Fisher's Exact Test				.432	.216
Linear-by-Linear Association	1.088	1	.297		
N of Valid Cases[b]	94				

Relationship between Protease inhibitors and adverse drug event

Crosstab

		Is Adverse drug event the type of DRP		
		Yes	No	Total
Is Protease inhibitors a class of ARV associated with DRP	Yes	2	3	5
	No	36	53	89
Total		38	56	94

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.000[a]	1	.984		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.000	1	.984		
Fisher's Exact Test				1.000	.679
Linear-by-Linear Association	.000	1	.984		
N of Valid Cases[b]	94				

Relationship between Protease inhibitors and non-compliance

Crosstab

		Is non-compliance the type of DRP		
		Yes	No	Total
Is Protease inhibitors a class of ARV associated with DRP	Yes	1	4	5
	No	37	52	89
Total		38	56	94

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.915[a]	1	.339		
Continuity Correction[b]	.238	1	.625		
Likelihood Ratio	.999	1	.317		
Fisher's Exact Test				.645	.324
Linear-by-Linear Association	.905	1	.341		
N of Valid Cases[b]	94				

Relationship between Protease inhibitors and no drug initiation

Crosstab

		Is no drug initiation the type of DRP		Total
		Yes	No	
Is Protease inhibitors a class of ARV associated with DRP	Yes	2	3	5
	No	16	73	89
Total		18	76	94

6. THE RATE OF INTERVENTIONS TO PREVENT OR RESOLVED DRUG RELATED PROBLEMS ASSOCIATED WITH HIV/AIDS PATIENTS.

Rate of Intervention involved to prevent or resolve DRP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	23	7.6	24.5	24.5
	No	71	23.5	75.5	100.0
	Total	94	31.1	100.0	
Missing	System	208	68.9		
Total		302	100.0		

Type of drug intervention involved

If Yes type of intervention involved to prevent or resolve DRP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Adherence counselling	8	2.6	34.8	34.8
	Change of drug	11	3.6	47.8	82.6
	Stopping of drug	4	1.3	17.4	100.0
	Total	23	7.6	100.0	
Missing	System	279	92.4		
Total		302	100.0		