TREATMENT FAILURE AND ASSOCIATED FACTORS AMONG INDIVIDUALS ON SECOND LINE ANTIRETROVIRAL THERAPY ATTENDING MBALE REGIONAL REFERRAL HOSPITAL: A RETROSPECTIVE COHORT STUDY

SAM MATEKHA

REG NO: BU/GS16/MPH/9

Supervisors: **1) Assoc Prof. Jayne Byakika-Tusiime**

2) Dr. John Peter Masette Masaba

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Declaration

I, Sam Matekha BU/GS16/MPH/9, declare that this dissertation is my original work except where due acknowledgement has been made in partial fulfillment for the award of the degree of Master of Public Health of Busitema University. I further declare that this dissertation has not been previously presented or submitted to this University as a research project or any other institution for partial fulfillment of any qualification.

Signature: …… Date……

Dedication

This work is dedicated to my parents Mr. and Mrs. Mulongo Stephen and my dear son, Elisha Jayden Matekha.

Acknowledgement

I thank all those who in one way or other contributed and supported this work.

First and foremost, I want to thank the Almighty God for his guidance, provision and protection.

I would like to thank most sincerely my supervisors - **Prof. Jayne Byakika- Tusiime and Dr. John Peter Masette Masaba** who tirelessly gave me support and guidance right from the start of this study to the end. Your academic and professional input made it possible for this study to be done.

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God bless you.

Dissertation Approval

This dissertation is submitted as a partial fulfillment for the award of the Masters' Degree in Public Health of Busitema University with our approval as supervisors.

1. Jayne Byakika-Tusiime, B Pharm, MSc, PhD

   Associate Professor of Epidemiology

   School of Health Sciences

   Department of Public Health

   Soroti University

   P O BOX 211 Soroti

   Uganda

SIGN…… DATE…12 December 2020……

2. Dr. John Peter Masette Masaba, MBChB, M MED (INTERN MED), FCP (ECSA)

   Senior Consultant Physician/ Lecturer

   Department of Internal Medicine

   Faculty of Health Sciences

   Busitema University

SIGN……. DATE…….

Acronyms and Abbreviations

3TC	Lamivudine
AIDS	Acquired Immune Deficiency Syndrome
ABC	Abacavir
ARVs	Antiretrovirals
ART	Antiretroviral Therapy
AZT	Zidovudine
CD4	Cluster of Differentiation Type 4
EFV	Efavirenz
FDC	Fixed Dose Combination
HIV	Human Immunodeficiency Virus
LPV/r	Lopinavir/ritonavir
NRTI	Nucleoside Reverse Transcriptase Inhibitors
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitors
NVP	Nevirapine
OIs	Opportunistic Infections
PI	Protease Inhibitor
PMTCT	Prevention of Mother to Child Transmission of HIV/AIDS
TB	Tuberculosis
TDF	Tenofovir
UNAIDS	The Joint United Nations Program on HIV/AIDS
WHO	World Health Organization

Operational Definitions

Second-line ART The ART regimen used for treatment of individuals living with HIV who have

failed on a first-line regimen, and typically consists of a PI (Atazanavir or ritonavir) and two or NRTIs.

Treatment Failure A rise in plasma viral load above 1,000 copies/mL in 2 consecutive viral load measurements, the first one being done at six months after switching to second line regimen, and the second one done four months after the first viral load measurement.

Virologic Failure When a PLHIV on antiretroviral therapy has persistently non-suppressed viral load exceeding 1000 copies/ml (two consecutive viral load measurements within a 6-month interval, with adherence support between the two measurements) after at least 6 months of starting a new ART regimen

Immunological Failure A fall in CD_4 cell count to baseline (or below) or a 50% reduction from treatment peak value or presence of persistent CD_4 cell count below 100 cells/mm^3

Clinical Failure An occurrence of new or recurrent WHO stage 4 or some stage 3 conditions in an HIV positive individual who was previously stable

Viral load coverage This refers to the proportion individuals on ART with a of documented viral load test in the last 12 months.

ABSTRACT

Background: ART failure is a growing public health problem and a major threat to the progress of HIV/AIDS control. In Uganda however, little is documented on treatment outcomes and their associated factors among individuals on second line ART regimen.

The rapid scale-up of ART over the past has resulted in substantial reductions in morbidity and mortality. However, as millions of people must be maintained on ART for life, individuals with ART treatment failure are increasingly encountered and the numbers are expected to rise. This could be attributed to factors such as sub-standard regimens, limited access to routine viral load monitoring, treatment interruptions, suboptimal adherence, among others. The purpose of this study was to estimate five-year cumulative treatment failure and the associated factors among individuals on second line ART regimen attending Mbale regional referral hospital.

Materials and methods: A retrospective analysis of 541 records of HIV positive individuals, switched to second line ART regimen from Jan 2012 to Dec 2017. Inferential statistics including the Chi square test and multivariable logistic regression analysis was applied to determine associations of treatment failure against of the selected demographic, laboratory and clinical factors was performed. Associations between treatment failure and the predictors was based on a p-value of less than 5% and confidence intervals level of 95%.

Results

We reviewed 541 records of individuals on second line ART regimen, of which 350 (64.7%) were female, 226 (41.8%) were married, and 197 (36.4%) were older than 35 years. The mean age at ART initiation was 30 years (SD=14. 8), while the mean weight at ART initiation was 47kgs (SD=18.6), (range 4-97 kgs).

The overall proportion of treatment failure was 23%. The cumulative mortality risk for five years was 12.4% and the mortality rate was 2.5 deaths per 100 individuals per year.

The odds of developing treatment failure among individuals switched to ATV/r-based regimen were 44 % lower as compared to individuals who were switched to LPV/r (OR_{adj}0.56, 95% CI 0.35-0.90, p=0.016). while the odds of experiencing treatment failure among individuals that used AZT at ART initiation were 43% lower as compared to individuals that used a TDF based regimen at ART initiation (OR_{adj}0.57, 95% CI 0.33-0.98, p=0.041).

Conclusion:

The five year cumulative incidence of treatment failure in a cohort of 541 individuals was 23%. The type of protease inhibitor (PI) used in second line regimen and use of AZT at ART initiation were significantly associated with treatment failure. Our study also shows that the cumulative mortality risk while on second line ART regimen was 12.4% while the mortality rate was 2.5 deaths per 100 individuals per year.

Recommendations:

The Ministry of Health should consider adopting early resistance testing for persons with viral loads beyond the threshold so as to facilitate early identification of resistance and subsequent regimen switch to higher regimens.

According to the 2018 HIV prevention and treatment guidelines, third line ART regimen is only issued at the regional referral hospitals. We recommend that an alternative third-line ART regimen be availed for those individuals in district hospitals who are on a failing second-line regimen given the high level of treatment failure among individuals on 2nd line ART regimen,