VALIDITY OF CLINICAL AND IMMUNOLOGICAL MONITORING TO DETECT VIROLOGICAL FAILURE IN HIV INFECTED CHILDREN ON ANTIRETROVIRAL THERAPY IN DAR ES SALAAM, TANZANIA, 2012

By

Edward Mgelea, MD

A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Medicine (Pediatrics and Child Health) of the Muhimbili University of Health and Allied Sciences

Muhimbili University of Health and Allied Sciences

October, 2012

CERTIFICATION

The undersigned certify that they have read and hereby recommended for acceptance by Muhimbili University of Health and Allied Sciences a thesis/dissertation entitled: ***The validity of clinical and immunologic monitoring in predicting virological failure among HIV infected children on ART in Dar es Salaam, Tanzania, 2012*** in fulfillment of the requirement for degree of Master of Medicine (Paediatrics and Child Health) of the Muhimbili University of Health and Allied Sciences.

_____

Dr Rodrick Kisenge

Supervisor

Date _____

_____

Prof Said Aboud

Supervisor

Date_____

DECLARATION

AND

COPYRIGHT

I, Edward Mgelea, declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other university for similar or other degree award.

Signature……

Date……

ACKNOWLEDGEMENT

Various people have contributed tirelessly to make this work possible, and I am sincerely appreciating the support from my supervisors. Laboratory Staff: Miss Mgaya, Mchaki and Theofrida.

Special thanks to MUHAS, MDH, and ICOTRA for the financial support to this valuable work. Thanks to the clinic staff, HIV infected children on ART and the caretakers of all centers I conducted data and sample collection.

Very special thanks to Prof E.F.Lyamuya and Prof S. Kaaya who at the beginning of protocol development gave the way to achieve the work at this level.

I would like to appreciate and thank the District Medical Officers (DMO`s) of the three municipals of Dar es Salaam for granting me permission to collect data at the municipal heath facilities.

Special thanks to all members of the Department of Pediatrics and Child Health, MUHAS and MNH for your support throughout this study.

My classmates (Drs: Robert Moshiro, Alex Mphuru, Issabella Sylvester, Julieth Kabengula, Fatou Secka,Winfred Kyambile, Richard Christopher, Gloria Mbwile, Charles Shija, Frida Mghamba). I thank you for your important contributions.

DEDICATION

I would like to dedicate this thesis to my Lovely daughter Endy, My wife Teddy for their sincere moral support during the entire period of this work. May Almighty God Bless you.

ABSTRACT

Background: Globally, it is estimated that 2 million children under the age of 15 years are living with human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) and the majority reside in sub-Saharan Africa, South and Southeast Asia.

In Tanzania, it is estimated that around 160,000 children are living with HIV and more than 11,000 children are on antiretroviral therapy (ART). The treatments response monitoring is primarily by using clinical and immunological parameters to detect virological failure. The validity of clinical and immunological monitoring to detect virological failure in children receiving ART is not well documented.

Objective: To determine the validity of clinical and immunologic monitoring in detecting virological failure among HIV infected children on ART in Dar es Salaam.

Methods: The study is health facility based cross sectional study of HIV infected children attending care and treatment clinics, who were receiving ART for at least six months. We screened 485 children on ART in Dar es Salaam for enrollment. 218 met inclusion criteria and blood samples were taken for viral load (VL) testing. Two hundreds and seventeen results were available for analysis. One VL results was inconclusive. The viral load testing was performed using Roche Cobas Amplicor HIV-1 RNA monitor version 1.5 assay (Roche Diagnostics, USA). Plasma VL below 400 copies/ml indicates good response to ART while Plasma VL ≥401 copies/ml defined Virological failure. SPSS version 17.0 and Epi Info Version 6.0. (CDC, Atlanta, USA) were used for statistical analysis. Chi square test was used to analyse categorical variables. Logistic regression was used to determine predictor of virological failure.

Results: Two hundred and eighteen children were included in the study. Overall mean age of the children was 10.6 years (range 1-16 years). Of 217 children with available viral load results, 124 (57.1%) had virological failure. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of clinical criteria were 12.9%, 90.3%,

64.0% and 43.8% respectively. The immunological criteria had sensitivity, specificity PPV and NPV of 22.6%, 73.1%, were 53.3% and 41.4% respectively. The combined clinical and immunological criteria has sensitivity of 25.8%, specificity 69.9%, while PPV and NVP were 53.3% and 41.4% respectively. Children who received NVP based regimens were more likely to have virological failure compared to other regimens, OR=2, 95% CI (1.20-3.64), *p=0.03*.

Conclusion: Virological failure was highest followed by immunological and clinical failures. This study demonstrated a poor performance of current recommended clinical and immunological criteria to monitor HIV-infected children on ART. Children who were on NVP-based regimens had a higher risk of developing virological failure than those who were in other regimens.

Recommendations: Improving access to viral load testing is feasible approach at this stage for early and reliable identification of virological failure in children on ART in order to make informed decision on switching to second line regimen. Regular surveillance on resistance test is recommended to detect early emergence of HIV drug resistance.

.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF ABBREVIATIONS

ARV`	ANTI RETROVIRAL
AIDS	AQUIRED IMMUNODEFICIENCY SYNDROME
ART	ANTI RETROVIRAL THERAPY
CTC	CARE AND TREATMENT CENTER
DNA	DEOXYRIBONUCLEIC ACID
ART	ANTIRETROVIRAL THERAPY
HIV	HUMAN IMMUNODEFICENCY VIRUS
EDTA	ETHYLENE DIAMINE TETRAACETIC ACID
MDH	MANAGEMENT DEVEPLOMENT FOR HEALTH
MUHAS	MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES
PCR	POLYMERASE CHAIN REACTION
PI	PROTEASE INHIBITORS
PPV	POSITIVE PREDICTIVE VALUE
NPV	NEGATIVE PREDICTIVE VALUE
NVP	NEVIRAPINE
RNA	RIBONUCLEIC ACID
VF	VIROLOGICAL FAILURE
VL	VIRAL LOAD
WHO	WORLD HEALTH ORGANISATION