INCIDENCE AND FACTORS ASSOCIATED WITH FIRST LINE ANTIRETROVIRAL TREATMENT FAILURE IN CHILDREN ATTENDING THE JOINT CLINICAL RESEARCH CENTRE KAMPALA, UGANDA

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ABSTRACT

Background

The human immunodeficiency virus (HIV) disease develops very rapidly among infants and children mainly due to the immature immune system. Without treatment, half of the children die before their second birthday. Therefore, there is need to start antiretroviral therapy (ART) early to prevent the avoidable deaths. Global access to antiretroviral therapy has risen considerably over recent years, however monitoring efficacy of treatment in resource limited settings is difficult due to reasons such as: limited laboratory facilities and shortage of trained staff. As a result early recognition of ART treatment failure remains a challenge.

Objective: This study aimed to describe the incidence and the factors associated with first line treatment failure among the children attending the Joint Clinical Research Centre (JCRC) paediatrics outpatient's clinic.

Methods: A retrospective Cohort with a nested case control study of HIV-1 positive children who had been initiated on ART between January 2004 and September 2009 under the Timetable for Regional Expansion of antiretroviral Therapy (TREAT) program at the JCRC was studied. Data of children aged 6 months up to 18 years who meet the eligibility criteria were extracted from the charts and the JCRC patient care database using a pretested data extraction tool. Data on the social demographic, WHO clinical stage, HAART initiation dates and laboratory follow up tests, were extracted. Kaplan-Meier survival curves and Cox regression models were used to estimate the factors, median time to ART treatment failure plus the incidence. The chi-square test and logistic regressions were used to determine the factors that are associated with treatment failure.

Results: A total of 701 children`s medical records were reviewed, 240(34%) failed on first line antiretroviral therapy (cases) and 461(66%) did not fail (controls).The overall median time to first line ART failure was (IQR) 26.4 (18.9-39.1) months of follow up, with different incidence rate ratios (IRR) for the commonly used first line ART regimens although the differences were not statistically significant n(95%) confidence interval(CI). Stavudine/lamivudine/nevirapine D4T/3TC/NVP)1.11(0.80-1.15)p=0.50, stavudine/lamivudine/efavirenz(D4T/3TC/EFV) 0.85(0.62-1.14)p=0.26, zidovudine/lamivudine/nevirapine(AZT/3TC/NVP) 1.07(0.79-

1.43)p=0.64 and zidovudine/lamivudine/efavirenz(AZT/3TC/EFV) 0.95(0.66-1.33)p=0.75 when each regimen was compared to the other three regimen respectively.

The factors that were associated with treatment failure were poor adherence [(OR= 6.74, 95 CI: 4.74-10.14) p<0.001], exposure to single dose nevirapine (sdNVP) [(OR=2.06, 95%CI:1.09-3.86), p=0.025] and NVP containing regimen [(OR=1.69,95%CI:1.13-2.53), p=0.011].

Among the genotypic resistance profiles analyzed, the commonest NNRTI resistance associated mutations (RAM) were: K103N (59; 54%)), Y181C (36; 27%)) and G190A (26; 24%)) while the commonest NRTI RAM was the M184V (89; 81%), thymidine analogue- mutations (TAMs) were in 20 % of patients.

Conclusion: The cumulative incidence rate of first-line ART virological failure in this study was 34% with a median time to failure of 26.4 months. Poor adherence to ART, sdNVP exposure and a NVP backbone NNRTI were associated with first line ART failure. The K103N and Y181C RAM for the NNRTIs and the M184V for NRTI were common mutations. However, the high level TAMs calls for Virological monitoring to avoid compromising second line options.

Recommendations: Adherence to ART should be further emphasized at all levels of care to ensure treatment success. In ART naïve children, an efavirenz based first line regimen as opposed to a nevirapine one should be used. Routine virological monitoring should be in-cooperated in paediatric ART programs especially after the first year of therapy to avoid accumulation of TAMs.