Journal of HIV for Clinical and Scientific Research

Adaora A Okechukwu[1]* and Frank I Amajuoyi[2]

[1]Infectious Disease Unit, Department of Paediatrics, University of Abuja Teaching Hospital, Gwagwalada, Abuja, Nigeria
[2]Special Treatment Clinic, Department of Paediatrics, University of Abuja Teaching Hospital, Gwagwalada, Abuja, Nigeria

Dates: **Received:** 18 July, 2015; **Accepted:** 08 September, 2015; **Published:** 10 September, 2015

***Corresponding author:** Dr. Adaora A Okechukwu, Department of Paediatrics, University of Abuja Teaching Hospital, Gwagwalada, PMB, 228, FCT-Abuja, Nigeria, Tel: +2348036719906; E-mail: nebokest@yahoo.com

www.peertechz.com

ISSN: 2455-3786

Keywords: Highly active antiretroviral therapy; CD4; Viral load; Weight

Research Article

First and Second Line Highly Active Anti-Retroviral Therapy Failure in HIV Infected Nigerian Children at University of Abuja Teaching Hospital Gwagwalada, Nigeria

Abstract

Background: In high-income countries, viral load is routinely used for monitoring HIV patients on antiretroviral therapy for early detection of drug failure. This is not the case in most resource limited settings like ours where only WHO immunological and clinical criteria are used for monitoring. This study is aimed at determining the rate/time of failure to 1st and 2nd antiretroviral drugs in children in our centers.

Method: Is a retrospective study of children ≤18 years switched to 2nd line antiretroviral regimen and those requiring third line drugs from Jan 2006 to June 2015 in our health institution. Data analysis was conducted using SPSS version 16.0 software and statistical significance set at $p < 0.05$.

Result: Sixteen percent (82/514) of children on 1st line medication were switched to 2nd line drugs with switch over rate of 9 persons/year, and 6/82 (7.3%) required 3rd line medication. The median switch over time was 31.3 months (IQR 26.4-36.2) for 2nd line medication, and 42.6 months (IQR 40.1-44.3) from time of switch to 2nd line drugs for those requiring 3rd line regimen. Over 90% of patients switched to 2nd line drugs were between 9-18 years, none was an infant. The mean CD4 cell count and viral load before switch to 2nd line drugs were 109.09±29.23 cell/mm^3 and 180,480.29±35,303 copies/ml, and 89.42±28.67 cell/mm^3/ 237,337.5±64,619 copies/ml for those requiring 3rd line medications. There was over 450 fold increase in viral load from the expected undetectable level of 400 copies/ml after 6 months on medication before patients were switch to 2nd line drugs, and over 590 folds increase for those that require 3rd line medications. Significant difference was seen in the mean CD4 cell count and weight of those with adherence of ≥ 95% and ≤ 95% (p values were <0.05).

Conclusion: WHO immunological and clinical criteria were found not to be ideal for monitoring of children on antiretroviral therapy. Six monthly viral load monitoring and resistance testing should be introduced in Nigerian guideline for managing HIV children for better therapeutic and pharmaco-economic outcomes. Third line medication should also be made available in the country and intensification of adherence is required in adolescent age group.

Introduction

Globally, over 3.4 million children were living with HIV at the end of 2011, 91% of whom are in sub-Saharan Africa [1]. Highly active antiretroviral therapy (HAART) has markedly reduced the morbidity and mortality of patients with HIV/AIDS [2,3], and has a major role of achieving and maintaining undetectable viral load (VL) of <400 copies/ml after 6 months on therapy [4]. While the number of children receiving HAART continues to increase [5], access to optimal laboratory monitoring with VL testing remains limited. For this reason, most health care providers in resource limited settings make decisions about commencement of these drugs and subsequent switch over to 2nd line regimen by the World Health Organization (WHO) immunologic and clinical guidelines without VL measurement [6-8], thus leaving HIV-infected children in those environment at risk of unrecognized virologic failure and the subsequent development of antiretroviral resistance. Switch to 3rd line medication is practically non-existence in most areas were routine VL monitoring is not place.

The WHO [6-8], and Nigerian Guidelines for Pediatric HIV and AIDS Treatment and Care [4], defined virological failure as VL not suppressed to undetectable levels (<400 copies/ml) after 6 months on antiretroviral therapy (ART), or a persistent increase in VL > 1000 copies/ml following a period of adequate suppression. The immunological indication for treatment failure is the development or return of CD4 cell count to <200cells/mm^3 or % CD4+ of < 10% for a child > 2years to < 5 years of age or CD4 cell count of <100cells/mm^3 for a child 5 years of age or older, or return of CD4 cell count to pre-therapy baseline level, or count of below 50% decline from on-therapy CD4 cell peak level [4,6-8]. The clinical indication for treatment failure is the development of either new or recurrent WHO stages 3 or 4 events in a child on therapy [4,6-8]. The virological failure occurs as first event, followed by immunological and clinical failure usually months or years afterwards [9]. If patients do not achieve an undetectable VL, viral replication ensures, this often leads to development of spontaneous random mutation in HIV genome [9].

The most concern finding is that the WHO immunologic criteria for treatment failure detected virologic failure in 1 of 16 children (6%) [9]. In adults, the criteria have been shown to be insensitive measures for virologic outcomes [10,11], and a high prevalence of ARV resistance mutations has been documented in HIV-infected adults by the time they progress to meet the WHO criteria for ARV therapy switch [12]. A recent report showed same similarity in pediatric WHO guidelines, where it has been found to offer an insensitive measure of virologic failure [13]. This was confirmed in Ugandan study by Ruel et al. [9], and additionally demonstrated that the HIV-infected African children with ongoing undetected virologic failure develop ARV-mutations that could compromise future therapeutic options.

Immunologic and virologic measures are the state of the art for monitoring ART and should be made available in all settings where HIV infection is treated. In resource-rich countries, the standard of care for monitoring treatment in HIV-infected children is the routine laboratory monitoring of CD4+ T cell percentage or count, and VL [14]. In USA, CD4+ T cell percentage or count and VL are measured at the time of diagnosis of HIV infection and at least every 3-4 months thereafter [15]. Due to the lack of accessible, costly technical equipment, complex technology, expensive reagents, poor laboratory infrastructure, and prohibitive maintenance cost, this test is not routinely available in many resource-limited settings [16]. The available commercial assays for VL determination costs between $50 and $100 per test making it unaffordable to many centers in resource-limited countries [17]. The WHO highly recommends national programs to develop the laboratory capacity for monitoring ART. However, in the absence of laboratory capacity (VL assay), immunological and clinical parameters are used for monitoring ART.

Growing number patients in the developing countries have switched to 2nd line therapy, and some requiring 3rd line medications [18-20]. Failure to 1st line ART has been documented in 13% of HIV-infected Uganda children [9], 16% in South Africa [21], 16% in Thailand [22], 33% in Kenya [23], 44% in Mali [24], 9.1% in another South African study [25], and 0.8% from a multi-center study in Africa and Asia [26]. Adherence to ARV therapy has a major role of achieving good viral suppression on HIV patients. For patients failing 2nd line therapy, treatment options are largely non-existent in most resource limited settings. The current WHO guidelines provide some guidance for treatment in the case of 2nd line failure, but financial constraints will limit the adoption of 3rd line options in countries with limited resources. Nigeria is one of the high HIV-burden countries in Africa, and has up to date made no provision for ART therapy beyond 2nd line in its national guidelines, and no provision for routine use of VL in monitoring patients on HAART [4]. Thus, there is a need to document the rate/time of failure to 1st and 2nd line regimen using WHO immunological and clinical failure. Such information is needed to evaluate the effectiveness of WHO immunological and clinical criteria, and provide baseline information on children failing these drugs. Such information is needed for optimal ARV management in the population.

Materials and Methods

It observational descriptive retrospective study, conducted at Pediatric Outpatient Special Treatment Clinic (POSTC) for HIV/AIDS children at the University of Abuja Teaching Hospital (UATH), Gwagwalada from January 2006 to June 2015. POSTC is an out-patient clinical service area where HIV infected children and exposed babies are followed up for treatment and monitoring. It has consulting rooms for the doctors, the nurses, and adherence counselors. Record clerks, pharmacists, and nutritionists are also at their disposal on week days (Monday-Friday, from 7.30 am to 4 pm.). UATH is a 350 bed capacity referral hospital, sub-serving the people of Federal Capital Territory (FCT) Abuja and five neighbouring states. Is one of the first centers to start offering free HIV/AIDS services in the country, through the President Emergency Plan for AIDs Relief (PEPFAR) since 2005.

The subjects were pediatric HIV infected patients' ≤18 years diagnosed by either by serological method or by deoxy-ribonucleic acid (DNA) polymerase chain reaction (PCR) test, started on 1st line ARV therapy and later switched over to 2nd line drugs. They all met WHO immunological and clinical criteria for commencement on 1st line ARV therapy, and were started on them according to the national guideline [4]. VL is not routinely done in our center before commencement on 1st line ARV therapy; it is only done at suspected immunological and clinical failure to 1st line medications, and most recently one year after the commencement of 2nd line medications or when there is immunological or clinical indication of non or slow response to 2nd line medication. The medical folders of all the patients switched to 2nd line ARV therapy were retrieved from the medical information department of the health institution and required information collected. They include: age of the patient at the commencement on 2nd line drugs, sex, type of 1st line and 2nd line regimen started, CD4 cell count at initiation of 1st line, CD4 cell count at subsequent periods of 6 months until the time of switch over to 2nd line drug and thereafter, their VL before and after the switch to the 2nd line regimen, and yearly subsequently. Their weight was also collected as their CD4 cell count. Also collected was adherence level as recorded by adherence counselors in their medical folders. Self-reporting by the parents/ caregiver of the patients, or the patients themselves in cases of adolescents, and keeping of appointment in the health facility were the methods used by adherence counselors in determining the level of adherence in our health institution, while the physicians uses weight, CD4 cell count and clinical parameters in following up their patients. Pill count and pharmacy refill were used by the pharmacists, while other methods eg mobile phone technologies, and electronic monitoring were not in use in our health facility. CD4 cell count was measured using automated Partec Cyflow easy count kit (*Partec code no. 05-8401 Western Germany*), VL measurement was with (*Roche Smp /prep /cobs Taqman 96, USA),* and Seca beam weighing scale accurate to the nearest 0.01kg was used for measuring their weight.

Ethics clearance was obtained from the Ethics Committee of the health institution before the commencement of the study. Data analysis was conducted using SPSS version 16.0 that produced frequencies, percentages, means, and standard deviations. The tests for associations and differences were done by student t-test, and statistical significance set at p value <0.05.

Results

Table 1 depicts the characteristics of the study population at initiation of 1st line HAART. A total of 82/514 (15.9%) patients, 48(58.5%) males and 34(41.5%) females were switched to 2nd line

Table 1: Characteristics of 82 children switched to 2nd line HAART.

Characteristics	Sex		Total
	Male	Female	
Sex	48(58.5)	34(41.5)	82(100.0)
*Age (years)	12.2±1.2	10.4±3.6	11.3±2.1
*Wt (kg)	19.1+6.3	17.8+4.2	18.5+5.3
Age Group (yrs)			
0 – <5	1(0)	0(0)	1(1.2)
5-< 10	10(52.6)	9(47.4)	19(23.2)
10-<15	28 (59.6)	19(40.4)	47(57.3)
>15-18	9(60.0)	6(40.0)	15(18.3)
*Pre 1st line CD4 cell			
count (cells/mm3)	116.74+33.71	85.36+24.94	101.58+29.32
*Pre2nd line CD4 cell			
count (cells/mm3)	120.04±32.06	98.15±26.39	109.09±28.37
*Pre 2nd line Viral load			
(copies/ml)	189,987.75 ± 40,161	170,974.88 ± 30,444	180,480.29 ± 35,303

HAART: Highly active anti-retroviral drug.
*Values are mean ± SD.

medications, while 6/82 (7.3%), with 3/6(50.0%) males and 3/6 (50.0%) females required 3rd line medication during the nine years review period. The average switch over rate for 2nd line drugs was 9 persons/year, and 2 persons per every 3 years for those requiring 3nd line medications. Median switch over time for 2nd line drugs was 31.3 months (IQR 26.4-36.2), and 42.6 months (IQR 40.1-44.3) from the time of switching to 2nd line drug for those requiring 3rd line regimen. Majority `of patients (90.4%) switched to 2nd line drugs and those requiring 3rd line medication were within the age bracket of 9 to 18 years, none was an infant and only 1(1.2%) under five. Their mean age, weight and CD4 cell count of the 82 subjects before commencement on 1st line HAART were 11.3±2.1years, 18.5±5.3kg, and 101.58±29.32 cells/mm^3, while their CD4 cell count and VL before 2nd line HAART were 109.09±28.37 cells/mm^3, and 180,887.29 ±54,628 copies/ml respectively. The 1st line ARV drugs used were: 36(43.9%) for combination of AZT + 3TC + NVP, 27(32.9%) for D4T + 3TC + NVP, 19(21.2%) for D4T + 3TC + EFV, while the 2nd line ARV drugs used were: 49 (59.8%) for ABC + didanosine (ddl) + LP/r, 24 (29.3%) for TDF + 3TC + LP/r, and 9(11.0%) for ABC + 3TC + LP/r, (data not shown).

CD4 cell count, and viral load of 6 subjects requiring 3rd line HAART

Table 2 showed the CD4 cell count, VL and outcome of the 6 subjects requiring 3rd line medications. There were 3/6 (50.0%) males with median switch over time of 42.6 months (IQR 41.1-43.3) from the start of 2nd line medication. Their mean CD4 cell count was 89.42±28.67 cell/mm^3, their VL which was also 237,337.5±64,619 copies/ml which has increased to over 590 folds at the time of immunological failure that occurred at mean period of 4.3 years of commencing 2st line HAART. With intensification of adherence there was marked reduction in VL of 2 (33.3%) subjects, 4/6 (63.3%) died inspite of improvement in adherence and non-availability/ affordability of 3rd line ARV drugs. It was also noted that the three deaths from failed 2nd line regimen received tenofovir, and died from HIVAN (HIV Associated Nephropathy), chronic renal failure, and HIV encephalopathy. Unfortunately resistance testing was not done in any of the patients because of non-availability and accessibility to laboratory services.

Pattern of CD4 cell count, weight, and viral load while on 1st and 2nd line HAART

Table 3 shows the pattern of CD4 cell count, weight and viral load changes during the 9 year review period while on 1st and 2nd line HAART for the 82 subjects that failed 1st line ARV therapy. The CD4 cell count doubled about the 6th month of initiation of 1st line HAART, tripled/ peaked by the 1st year before the gradual decline, and return to base line level between the 3rd-4th years. Though the mean pre 1st line HAART weight of 82 patients that failed 1st line drugs was 18.5±5.3 kg below the 5th percentile for their age using NCHS growth chart [27], it however increased at initiation of HAART, but never showed a downward trend even when the CD4 cell count had started declining and returning to baseline level at the 3rd and 4th year on medication. It is worth noting that at the time of immunological failure, the VL has increased to more than 450 folds above the 400 copies/ml recommended undetectable viral level after 6 months on ARV therapy, and this occurred at about 3.5 years after commencing 1st line HAART.

CD4 cell count, VL and weight Vs adherence level before 2nd Line HAART

Table 4 shows CD4 cell count, VL, and weight of patients before switch to 2nd line HAART, and their adherence levels. There was statistical significant difference in the mean values of CD4 cell count and weight for those with adherence of ≥95% and those with ≤ 95% (p values were 0.024 for CD4 cell count, and 0.038 for weight). However no difference was seen in their viral load, p value 0.103. The mean VL of 187,676.72 ±32,963.2 copies/ml of those with adherence level of ≥95% in this study was found to be over 450 fold greater than the recommended 400 copies/ml for adequate viral suppression when adherence is ≥95%.

Discussion

The present study showed switch over rate to 2nd line ARV drugs of 15.9% in our health institution over a 9 year review period. This was similar to the reported rate in some other resource limited settings

Table 2: Clinical characteristics of 6 patients for 3rd line Medications.

	Age	Sex	WHO stage	Duration of 2nd line (yrs)	Co morbidity	2nd line regimen Used	Mean VL copies/ml	Outcome
1	18	M	III	4.5	CRD	TDF,3TC, LP/r	336,688	Died
2	16	F	IV	4.0	HIVAN	TDF, 3TC, LP/r	300,296	Died
3	10	F	IV	3.5	HIVAN	ABC, 3TC, LP/r	312,732	Died
4	12	M	IV	5.3	HE	TDF, 3TC, LP/r	274,662	Died
5	15	M	IV	4.5.	DTB	TDF,3TC,LP/r	101,424	Alive
6	11	F	111	4.3	MUMP	ABC, 3TC,LP/r	98,223	Alive

CRD (Chronic Renal Disease),
HIV (Human Immune Deficiency Virus),
HIVAN (HIV Associated Nephropathy)
HE (HIV Encephalopathy),
DTB (Disseminated Tuberculosis).

Table 3: Pattern of CD4 cell count, weight and viral load while on 1st line and 2nd line HAART.

Charateristics	Before 1st line Drugs	After 1yr on 1st line	After 2yrs	After 3yrs	Before 2nd line Drugs	After 1yr on 2nd line	After 2yrs	After 3yrs	After 3.5yrs
*Age (yrs±SD)	11.3±1.2.				14.3±1.0				18.3±1.0
*CD4 Count (Cells/mm3±SD)	101.58+29.32	508.89±53.3	463.76±73.4	246.48±48.4	109.095 ±29.23	454.3±37.7	591.3 ±40.9	290.3 ±52.8	89.042 ±28.67
*Viral Load (Copies/ml±SD)	-	-			180,480.29±35,303	<20	<20	420.65 ±29.43	193,457.29 ±64,619
*Weight (kg±SD)	18.5 ±5.3	23.5 ±7.0	26.8 ±11.9	29.0 ±4.6	32.1 ±5.6	37.7 ±11.2	42.3 ±9.3	45.2 ±7.2	46.1 ±10.5

*Values are mean ± SD.

Table 4: CD4 cell count, weight, viral load and levels of adherence before 2nd line HAART.

Characteristics	Adherence		Total	P value
	<95%	>95%		
Number of subjects	43	39	82	
*CD4 Cell Count(cells/mm^3) *Viral load(copies/ml) *Weight (kg)	98.12 + 25.23 173,283.66 + 37,643.1 28.4 + 7.1	120.07 ± 33.21 187,676.72 + 32,963.2 31.3 + 4.1	109.095 180,480.29	0.024 ± 29.23 0.103 ± 35,303 32.1 ± 5.6 0.038

*Values are mean ± SD.

were HIV RNA VL assays was not routinely used in the monitoring of patients on ART; 13% in Uganda children [9], 16% in South Africa [21], 16% in Thailand [22], but fair much lower than 33% in Kenya [23], and 44% in Mali [24]. It was however higher than 9.1% reported from another South African study [25], and 0.8% from a multi-center study in Africa and Asia [26]. In the present study also, over 7.0% children had failed 2nd line medication, they had a mean VL of 237,337.5±64,619 copies/ml with over 590 fold increase thus posing a serious cause for concern in view of non provision/availability/affordability of 3rd line medications in Nigerian guideline and in most resource limited settings. This finding underscores the need for VL monitoring in patients on ARV therapy for early detection of virological failure and early switch of patients to 2nd line drugs in order to prevent persistent viraemia which is a good predictor for rapid development of ARV resistance mutations [9]. Third line ARV medications should also be made available in resource limited countries as growing number of children have started failing 2nd line medications. This is necessary to prevent untimely death and spread of résistance virus. If we continue relying on WHO recommended immunological failure before switch over to 2nd line medications, which occurred at a VL of 180,480.29±35,303 copies/ml in this study, it might infer that many of the children were VL is not routinely use for monitoring of patients on ARV therapy will be left with undetected persistent viraemia and subsequent development of multiple TAMs resistant viral strain. This will not only jeopardize the activity of thymidine analog ARVs use in second line regimen, but foster other mutations that will threaten the efficacy and reliability of second line regimens [9]. Resistant testing at this point is also supposed to be done prior to switch to either 2nd or 3rd medication for this will help in the detection of resistance virus, and guide in the choice of 2nd or 3rd medication. In view of the above findings in this study, though the sample was not large enough for inference, the recommended Nigerian guideline for monitoring of patients on ART should possibly be reviewed to add VL measurement before commencement of 1st or 2nd line ARV therapy and 6monthly

Citation: Okechukwu AA, Amajuoyi FI (2015) First and Second Line Highly Active Anti-Retroviral Therapy Failure in HIV Infected Nigerian Children at University of Abuja Teaching Hospital Gwagwalada, Nigeria. J HIV Clin Scientific Res 2(2): 049-054. DOI: 10.17352/2455-3786.000014

thereafter for monitoring purpose. Viral resistance testing should also be included in the national guideline before switch to 2nd or 3rd line medication. Inclusion of VL in the monitoring process, and resistance testing will not only ensure failure identification in patients at least within one year of starting ARV therapy but also will guide in the choice of 2nd or 3rd line. In the light of the above evidence, using VL monitoring and resistance testing will be cost-effective intervention that has proved successful in industrialized countries, and suppressed VL means less HIV transmission, and successful ART.

The clinical indication for treatment failure is the development of either new or recurrent WHO stages 3 or 4 events in a child on therapy [4,6-8]. With such development, one expects reduction in weight of the patients from chronic opportunistic infections. In the present study, even when immunological failure has occurred, weight reduction was not remarkable. Studies have shown that virological failure occur first, followed by immunological and clinical failure usually months or years afterwards [9,10]. Using only clinical failure and possibly weight loss which usually occurs months or years after immunological failures as the only criteria for switch to a 2nd line regimen as practiced in some resource limited settings also implies that the HIV-infected children in these areas will be left with ongoing undetected virologic failure. The maintenance of such children and adults on these failed drugs for years before waiting for WHO stage 3 or 4 symptoms to appear with accompanying weight reduction is a great opportunity for accumulation of resistance mutation of virus that will not only compromise future therapeutic options, but also risk of transmission of these mutant virus in future.

WHO defines adherence as the extent to which a person's behaviour in taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider [28]. It remains the major tool in achieving VL suppression, prevent drug resistance, and maintain the health of HIV infected patients. An adherence level of ≥ 95% is the accepted level for achieving good viral suppression [29,30], and missing drugs for as little as 2 days in a month can lead to an increase in VL, and development of mutant viral strains [31,32]. Such high level of adherence is required because of the rapid replication and mutation rate of HIV [33]. Adherence is the second strongest predictor of progression to AIDS and death in a person living with HIV, the first being the CD4 count [34]. Patient self-reporting is one of the most common methods used in assessing adherence in resource poor settings [35]. It measures adherence via the use of self-administered or interviewer-administered questionnaires and interviews [35]. The reliability and validity of this method depend on patients or caregiver/parents memory recall, honesty, and social desirability [35,36]. The other methods include: pharmacy refill records, pill count, VL monitoring, CD4 cell count, appointment keeping, electronic monitoring, and mobile phone technologies [28,30,35,36]. In this study, keeping of appointment with the clinic, self-reporting and CD4 cell count were majorly used by the adherence counselors in our health institution in the assessment of adherence level of the patients. There was statistical significant difference in CD4 cell count and weight of patients having good adherence of ≥ 95% and those with poor adherence of ≤ 95% in this study. This is similar with findings from other studies [35,36], but having no significant difference in VL in this two groups is in contrast to finding elsewhere [35,36], and could be because VL was not routinely used in the monitoring of patients in our study. The mean VL of 187,676.72 ±32,963.2 copies/ml of those with adherence level of ≥95% was found to be over 450 fold greater than the recommended 400 copies/ml when adequate viral suppression occur with adherence of ≥95%. This finding in this study buttresses the inadequacy of using CD4 cell count and other adherence monitoring tools without VL in the monitoring/assessing of patients on ART. Because virology failure occur first, months or years before immunological/clinical failure, using other adherence monitoring tools without VL means that those failing ART will be detected much more latter inspite of their been recorded as having good adherence or doing well on their ARV drugs.

The importance of adherence in maintaining good viral suppression should be stressed tirelessly, before the introduction of the first line drugs as well as during every following visit. Adherence in adolescents has been reported to be poorer than in younger children, and older adults in both resourced rich and limited settings [18]. Reasons include adolescents' risk taking behavior, the stage of development when thought and reasoning is not fully developed, and regimen fatigue [18,38]. As perinatally infected HIV children who have been on ARVs grow into adolescence, adherence was found to decrease because of long period on medication [18,19,36-38]. Some studies have reported adherence rates for long term prescription medications to be between 50–75% [18,19]. In the present study, adolescents between 9-18 years (90.4%) were switched to 2nd line medications, thus bringing into focus the issue of adherence to medications among adolescent, and the need to find a lasting solution to this reoccurring decimal. Introduction of Direct observational therapy (DOTs) strategies should be considered as a very important option in mitigation of this ugly trend in adolescents.

Conclusion

WHO immunological and clinical criteria were found not to be adequate in determining when to switch patients to 2nd line and 3rd line medications. Six monthly VL monitoring and resistance testing should be introduced in Nigerian guideline for monitoring of HIV children on ART for better therapeutic and pharmaco-economic outcomes. Third line medication should also be made available for them, and intensification of adherence in adolescents is required to minimize the risk of non-adherence in this age group.

Limitation of the Study

Owing to the small sample upon which the results were based, it is recommended that similar investigations be carried out in other centers in the country.

References

1. WHO (2014) Treatment of children living with HIV. WHO, Geneva, Switzerland.

2. Palella FJ Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, et al. (1998) Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. New Eng J of Med 338: 853-860.

3. Holtgrave DR (2005) Causes of the decline in AIDS deaths, United States, 1995-2002: Prevention, treatment or both? Int J of STD & AIDS 16: 777-781.

4. Federal Ministry of Health Nigeria (2010) National guidelines for paediatric HIV and AIDS treatment and care.

5. WHO (2006) Antiretroviral therapy of HIV infection in infants and children in resource-limited settings: Towards universal access. WHO; Geneva.

6. WHO (2008) Report of the WHO Technical Reference Group. Paper presented at: Paediatric HIV/ART Care Guideline Group Meeting; Geneva, Switzerland. April 10-11.

7. WHO (2010) Antiretroviral therapy of HIV infection in infants and children: Towards universal access: Recommendations for a public health approach-2010 revision. WHO; Geneva, Switzerland.

8. WHO (2010) Antiretroviral Therapy for HIV infection in adults and adolescents: recommendations for a public health approach-2010 revision. Geneva: World Health Organization.

9. Ruel TD, Kamya MR, Pasutti PW, Charlebois ED, Liegler T, et al (201l) Early virological failure and the development of antiretroviral drug resistance mutations in HIV-infected Ugandan children. J Acquir Immune Defic Syndr 56: 44-50.

10. van Oosterhout JJ, Brown L, Weigel R, Kumwenda JJ, Mzinganjira D, et al. (2009) Diagnosis of antiretroviral therapy failure in Malawi: poor performance of clinical and immunological WHO criteria. Trop Med Int Health 856–861.

11. Moore DM, Awor A, Downing R, Kaplan J, Montaner SG, et al. (2008) CD4+ T-cell count monitoring does not accurately identify HIV-infected adults with virologic failure receiving antiretroviral therapy. J Acquir Immune Defic Syndr 49: 477–484.

12. Hosseinipour MC, Van Oosterhout JJ, Weigel R, Phiri S, Kamwendo D, et al. (2009) The public health approach to identify antiretroviral therapy failure: high-level nucleoside reverse transcriptase inhibitor resistance among Malawians failing first-line antiretroviral therapy. AIDS 23: 1127–1134.

13. Emmett SD, Cunningham CK, Mmbaga BT, Emmett SD, Cunningham CK, et al. (2010) Predicting Virologic Failure Among HIV-1-Infected Children Receiving Antiretroviral Therapy in Tanzania: a Cross-Sectional Study. J Acquir Immune Defic Syndr 54: 368-375.

14. Mellors JW, Muñoz A, Giorgi JV, Margolick JB, Tassoni CJ, et al. (1997) Plasma viral load and CD4+ lymphocytes as prognostic markers of HIV-1 infection. Annals of Internal Medicine 126: 946–954.

15. Guidelines for the Use of Antiretroviral Agents in Paediatric HIV Infections.

16. Diagbouga S, Chazallon C, Kazatchkine MD, Van de Perre P, Inwoley A, et al. (2003) Successful implementation of a low-cost method for enumerating CD4 + T lymphocytes in resource-limited settings: the ANRS 12-26 study. AIDS 17: 2201–2208.

17. Katzenstein D, Laga M, Moatti JP (2003) The evaluation of the HIV/AIDS Drug Access Initiatives in Côte D'ivoire, Senegal and Uganda: how access to antiretroviral treatment can become feasible in Africa. AIDS 17: S1–S4.

18. Hamers R, Wallis CL, Kityo C, Siwale M, Mandaliya K, et al. (2011) HIV-1 drug resistance in antiretroviral-naive individuals in sub-Saharan Africa after rollout of antiretroviral therapy a multicentre observational study. Lancet Infect Dis 750-759.

19. Hoen E, Berger J, Calmy A, Moon S (2011) Driving a decade of change HIV/AIDS, patents and access to medicines for all. J Int AIDS Soc 14: 15.

20. Long L, Fox M, Sanne I, Rosen S (2010) The high cost of second-line antiretroviral therapy for HIV/AIDS in South Africa. AIDS 24: 915–919.

21. Reddi A, Leeper SC, Grobler AC, Geddes R, France K, et al. (2007) Preliminary outcomes of a paediatric highly active antiretroviral therapy cohort from KwaZulu-Natal, South Africa. BMC Pediatr 17: 7-13.

22. Jittamala P, Puthanakit T, Chaiinseeard S, Sirisanthana V (2009) Predictors of virologic failure and genotypic resistance mutation patterns in Thai children receiving non-nucleoside reverse transcriptase inhibitor-based antiretroviral therapy. Pediatr Infect Dis J 28: 826–830.

23. Wamalwa DC, Farquhar C, Obimbo EM, Selig S, Mbori-Ngacha DA, et al. (2007) Early response to highly active antiretroviral therapy in HIV-1-infected Kenyan children. J Acquir Immune Defic Syndr 45: 311–317.

24. Germanaud D, Derache A, Traore M, Madec Y, Toure S, et al. (2010) Level of viral load and antiretroviral resistance after 6 months of non-nucleoside reverse transcriptase inhibitor first-line treatment in HIV-1-infected children in Mali. J Antimicrob Chemother 65: 118-124.

25. Zanoni BC, Sunpath H, Feeney ME (2012) Pediatric Response to Second-Line Antiretroviral Therapy in South Africa. PLoS ONE 7: e49591.

26. Sauvageot D, Schaefer M, Olson D, Pujades-Rodriguez M, O'Brien DP (2010) Antiretroviral therapy outcomes in resource-limited settings for HIV-infected children <5 years of age. Pediatrics 125: e1039-1047.

27. Hamill PV, Drizd TA, Johnson CL, Reed RB, Roche AF, et al. (1979) Physical growth, National Centre for Health Statistics percentiles. Am J Clin Nutri 32: 607- 629.

28. Jani AA (2004) Adherence to HIV Treatment Regimens: Recommendations for Best Practices

29. Chesney MA (2006) The elusive gold standard: future perspectives for HIV adherence assessment and intervention. J Acquir Immune Defic Syndr 43: S149-S155.

30. Paterson DL, Swindells S, Mohr J, Brester M, Vergis E, et al. (2000) Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Ann Intern Med 133: 21-30.

31. Rand CS, Weeks K (1998) Measuring adherence with medication regimens in clinical care and research. In: Shumaker SA, Schron EB, Ockene JK, McBee WL, editors. The Handbook of Health Behavior Change. 2. New York: Springer Publishing Company, Inc; 1998. 114-132.

32. Vanhove G, Schapiro J, Winters MA, Merigan TC, Blaschke TF, (1996) Patient adherence and drug failure in protease inhibitor monotherapy (letter). JAMA 276: 1955-1956.

33. World Health Organisation (2003) Adherence to Long Term Therapies. WHO Switzerland.

34. Garcia de Ollala P, Knobel H, Carmona A, Guelar A, Lopez Colomes JL, et al. (2006) Impact of adherence and highly active antiretroviral therapy on survival in HIV infected patients. J Acquir. Immune. Defic Syndr 30: 105-110.

35. Merzel C, VanDevanter N, Irvine M (2008) Adherence to antiretroviral therapy among older children and adolescents with HIV: a qualitative study of psychosocial contexts. AIDS Patient Care STDS 22: 977 - 987.

36. DiMatteo MR, Giordani PJ, Lepper HS, Croghan TW (2002) Patient adherence and medical treatment outcomes: a meta-analysis. Med Care 40: 794-811.

37. Gilks CF, Crowley S, Ekpini R, Gove S, Perriens J, et al. (2006) The WHO public-health approach to antiretroviral treatment against HIV in resource-limited settings. Lancet 368: 505-510.

38. Ugwu R, Eneh EA (2013) Factors influencing adherence to paediatric antiretroviral therapy in Port Harccourt, South-South Nigeria. Pan Afr Med J 16: 30.

Citation: *Okechukwu AA, Amajuoyi FI (2015) First and Second Line Highly Active Anti-Retroviral Therapy Failure in HIV Infected Nigerian Children at University of Abuja Teaching Hospital Gwagwalada, Nigeria. J HIV Clin Scientific Res 2(2): 049-054. DOI: 10.17352/2455-3786.000014*