Discordant responses to highly active antiretroviral therapy in HIV-I infected subjects at the Nnamdi Azikiwe University Teaching Hospital Nnewi

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Highly active antiretroviral therapy allows for the reconstitution of immune functions however, discrepant responses may occur. A cross sectional study involving 50 HIV-I infected subjects randomly recruited from the HIV Clinic of Nnamdi Azikiwe University Teaching Hospital, Nnewi was conducted. Ethical approval and informed consent were obtained and blood samples collected. The following were determined; HIV-I screening and confirmation, CD4 count, Viral RNA extraction, viral load, amplification and gel electrophoresis. Data were analysed using SPSS version 20. In all, 2(4%) showed a favorable response, while 18(36%) failed on treatment. The mean CD4 count of 100.61±49 observed in failed response was significantly different from the 675.00±348 observed in favorable response (P < 0.05). Moreover, 12(24%) experienced Type I dissociation while 10(20%) experienced Type II dissociation .The difference between the CD4 counts and viral load levels of both the Type I and Type II dissociation were significant (P < 0.05). One sample was amplifiable out of the 50 HIV RNA extracts subjected to PCR for antiretroviral drug resistance testing. Discordant responses to Highly active antiretroviral therapy exists significantly in the population studied, therefore, adequate measures need to be put in place to reduce its level of occurrence.

Key words: HAART, viral load, RNA, discordant, response.

INTRODUCTION

Although, the primary goal of HAART is to suppress plasma HIV-1 RNA level (viral load, VL) below the level of detection within three to six months of starting therapy and to maintain it for the rest of the patient's life (BHIVA, 2001), there are other important goals of HARRT including restoring and preserving immunologic function, reducing HIV-related morbidity and mortality, improving quality of life and reducing vertical transmission (Boyd,
The criteria to define ART failures are not uniform. According to WHO (WHO, 2006), there are three definitions: clinical failure when there is a recurrent WHO stage 4; immunologic failure when CD4 falls to below the pre-therapy baseline, or below 50% of the on-peak value, or is persistently < 100 cells/mm; virologic failure when plasma VL >10000 copies/ml; Virologic success when VL is < 400 or 50 copies/ml (depending on the type of the assay) after six months of treatment (WHO, 2006). A cross sectional study was conducted among attendees in the HIV clinic of Nnamdi Azikiwe University Teaching Hospital, Nnewi. Informed consent was obtained from the participants after which they were served questionnaires. The following parameters were performed for each participant; HIV- screening and confirmation, CD4 count, Viral RNA extraction, viral load assay, and amplification and gel electrophoresis.

**Inclusion criteria**

1. HIV-I infected on HAART therapy for at least a period of 1 year.
2. Age range of 15-70 years.

**Exclusion criteria**

1. Patients were excluded if they test negative to HIV-I.
2. If they are not on drugs.
3. If they are drug experienced but duration is less than 1 year.
4. Pregnant women (After performing a pregnancy test for those not visibly pregnant and excluding those visibly pregnant).

**Study area**

The study area was Nnewi in Anambra state, Nigeria. The town is located within the tropical rain forest. Nnewi is located east of river Niger and 22 kilometers from Onitsha.

**Calculation of sample size**

Sample size was calculated using the minimum sample size for simple proportion with 5% margin of error and 95% level of confidence as shown below. Equally, a monthly prevalence rate (P) was obtained from the HIV clinic of the Nnamdi Azikiwe University Teaching Hospital, Nnewi.

\[
N = \frac{Z^2 \times P \times (1-P)}{D^2}
\]

Where \(Z=\) Standard normal deviation at 1.96(which corresponds to 95% confidence interval).

\(P = \) Monthly Sero prevalence of HIV infection in HIV clinic attendees =16%

\(Q = 1-P\)

\(D = \) Degree of accuracy/ precision expected = 0.05%

Substituting for the above formulae

\(N = 1.96^2 \times (0.16 \times 0.84) / (0.05)^2 = 206\)

**Sampling procedure and sample size**

Due to cost, 50 subjects were recruited from the sample population, using stratified random sampling technique by

**MATERIALS AND METHODS**

**Study design**

A cross sectional study was conducted among 50 HIV-I infected persons randomly recruited from the HIV Clinic of Nnamdi Azikiwe University Teaching Hospital, Nnewi. Ethical consideration was gotten from the Ethical Committee of Nnamdi Azikiwe University Teaching Hospital, Nnewi.
selecting every 4th subject.

HIV rapid testing

This was done using the serial testing algorithm and rapid HIV test kits consisting of Determine kit (Abbott Laboratories, USA), Unigold (Trinity Biotech, Ireland), Stat pak (Chembio Diagnostic System, USA) were used.

CD4 COUNT

The CD4+ T cell count was done to determine the level of immune function. The Cyflow Partec machine (Partec GmbH, Münster, Germany) was used.

Viral load assay using the Roche Amplicor HIV-1 monitor test version 1.5

The AMPLICOR HIV-1 MONITOR Test was used. It is based on five major processes which include Specimen preparation, reverse transcription (RT) of target RNA to generate cDNA, PCR amplification of target cDNA using HIV-1 specific complimentary primers, hybridization of the amplified products to oligonucleotide probes specific to the target(s), and detection of the probe bound amplified products by colorimetric determinations.

RNA extraction for drug resistance testing

This was done using Zymo Research Quick-RNA Micro Prep catalog NO R1050. It is an innovative product designed for the easy, reliable and rapid isolation of up to 5ug total RNA from blood, cultured cells or tissue samples.

RNA quantification

This was done using the nanodrop spectrophotometer v3.7

Primers

The region encoding the protease protein and part of the reverse transcriptase (RT) protein (Pro/RT)(1.1kb) was amplified using nested PCR with the following as outer primers: POLF1 (5’- CWTTRGARGAAATGATGACAGC-3’) and CAMPOLR2 (5’TTCCTCTGCCAATTCTAATTCTGC-3’), followed by POLF3 (5’RGARCAAGAGCCCAMCAGC-3’) and CAMPOLR1 (5’CCTGSATAAATCTGACTTCC-3’) as inner primers (Lar et al., 2007).

Reverse transcription polymerase chain reaction

This was performed using Thermo scientific verso 1-step RT-PCR Reddy Mix kit. Verso™ 1-Step RT-PCR Reddy Mix™ kit contains all the components required to perform a rapid, sensitive and reproducible RT-PCR for the detection and analysis of RNA.

Nested PCR (Second round amplification reaction)

This was performed using Go Taq Green master mix PCR reagent by Promega. Go Taq Green Master Mix is a premixed ready to use solution containing bacterially derived Taq DNA polymerase, dNTPs, MgCl and reaction buffers at optimal concentrations for efficient amplification of DNA templates by PCR.

Gel electrophoresis

Electrophoresis of the amplicons was done using agarose gel electrophoresis machine (EDVOTEK) and the bands were visualized using an EDVOTEK UV illuminator and gel pictures were taken with UV gel documentation system.

RESULTS

In Table 1, 2(4%) showed a favorable response (VL+/CD4) while 18(36%) failed on treatment with a mean CD4 count of 100.61 ± 49 as against that of favorable response with a mean CD4 count of 675.00 ± 348. For the discordant responses, 12(24%) are experiencing immunological failure (Type I dissociation) with mean CD4 count of 162.42 ± 137 and favorable virological response with mean viral load count of 400.00±00 copies per ml. Those with type II dissociation (10[20%]) fail to achieve reduced viral load levels despite ongoing immune reconstitution with mean CD4 count of 348.00±190cells/ mm3 and viral load levels of 48320.40 ± 46387. The CD4 count and viral load of eight subjects were unclassified since they did not meet the criteria for the drug response described in this study.

Findings from Table 2 shows that women 11(61.1%) failed more on HAART than men 7(38.9%). There were more women 8(66.7%) in the Type I dissociation response than men 4(33.3%). Subjects with favorable response had a geometric increase in CD4 count from baseline of 225.50 ± 35 to 675.00 ± 347 within 3 years on HAART while the failure group had a marginal increase in CD4 count from baseline of 96.88 ± 66 to 100.61 ± 49 after 3 years and 2 months on HAART. The current CD4 count and current viral load levels were significantly associated with type of response to HAART.

Results from Table 3 shows that males were better immunological responders than females with CD4 count increases from baseline of 128.47 ± 89 to 248.68 ± 267 while that of females increased from 162.51 ± 149 to
Table 1. Types of response to HAART and viroimmunological marker values in the study population.

<table>
<thead>
<tr>
<th>Marker of response</th>
<th>Favourable N=2/50</th>
<th>Failure N=18/50</th>
<th>p-value</th>
<th>Type I N=12/50</th>
<th>Type II N=10/50</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 Cells/mm³</td>
<td>675.00±348</td>
<td>100.61±49</td>
<td>0.000</td>
<td>162.42±137</td>
<td>340.00±190</td>
<td>0.020</td>
</tr>
<tr>
<td>VIRAL LOAD Copies/ml</td>
<td>400.00±0</td>
<td>63643.50±62010</td>
<td>0.176</td>
<td>400.00±00</td>
<td>48320.40±46387</td>
<td>0.002</td>
</tr>
<tr>
<td>Total</td>
<td>2(4%)</td>
<td>18(36%)</td>
<td></td>
<td>12(24%)</td>
<td>10(20%)</td>
<td></td>
</tr>
</tbody>
</table>

Results are presented as Means ± S.D. P value is significant at P < 0.05.

Table 2. Association between the type of response to HAART and sex, baseline CD4 count, current CD4 count, current viral load and duration on HAART.

<table>
<thead>
<tr>
<th>Type of response to HAART</th>
<th>Sex</th>
<th>Baseline CD4 count (cells/mm³)</th>
<th>Current CD4 count (cells/mm³)</th>
<th>Current viral load (copies/ml)</th>
<th>Duration on HAART (Yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male N (%)</td>
<td>Female N (%)</td>
<td>Baseline</td>
<td>Current</td>
<td>Current</td>
</tr>
<tr>
<td>Type I</td>
<td>4(33.3%)</td>
<td>8(66.7%)</td>
<td>179.25±119</td>
<td>162.42±137</td>
<td>400.00±00</td>
</tr>
<tr>
<td>Type II</td>
<td>5(50%)</td>
<td>5(50%)</td>
<td>144.10±112</td>
<td>340.00±190</td>
<td>48230.40±46387</td>
</tr>
<tr>
<td>Favorable</td>
<td>1(1%)</td>
<td>1(1%)</td>
<td>225.50±35</td>
<td>675.00±347</td>
<td>400.00±00</td>
</tr>
<tr>
<td>failure</td>
<td>7(38.9%)</td>
<td>11(61.1%)</td>
<td>96.88±66</td>
<td>100.61±49</td>
<td>63643.00±62010</td>
</tr>
<tr>
<td>Unclassified</td>
<td>2(25%)</td>
<td>6(75%)</td>
<td>211.62±231</td>
<td>263.25±195</td>
<td>2735.50±1595</td>
</tr>
<tr>
<td>P-value</td>
<td>0.840</td>
<td>0.189</td>
<td>0.000</td>
<td>0.001</td>
<td>0.506</td>
</tr>
</tbody>
</table>

Table 3. Gender difference in current CD4 count, baseline CD4 count and current viral load.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Current CD4 (cells/mm³)</th>
<th>P-value</th>
<th>Baseline CD4 (cells/mm³)</th>
<th>P-value</th>
<th>Current viral load (copies/ml)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male N=19</td>
<td>248.68±267</td>
<td>0.302</td>
<td>128.47±89</td>
<td>0.373</td>
<td>39163.68 ± 42616</td>
<td>0.516</td>
</tr>
<tr>
<td>Female N=31</td>
<td>190.03±129.09</td>
<td></td>
<td>162.51±149</td>
<td></td>
<td>29424.54 ± 55497</td>
<td></td>
</tr>
</tbody>
</table>

190.03 ± 129.09, though there were no significant difference in the values between males and females P > 0.05. Males, however, had more viral load count than females.

Here in Table 4, the relationship between sex and Type I and II responses were not significant with P > 0.05. In the drug classification, there is no significant relationship between the type of drug the patient takes and the discordant response to that drug. However, those with Type II dissociation were mostly on Protease inhibitor combination i.e. 2NRTI + PI (3 [30%]) and NRTI+ NNRTI + PI (6 [60%]) with only 1 (10%) taking the 2NRTI+NNRTI combination. Those with Type I and Type II responses predominate in the 25-44 age bracket with 8(66.7%) in the Type I group and 10(100%) in Type II. The age of an individual has a significant relationship with Type I and Type II responses with P < 0.05.

In plate 1, only one sample was amplified out of the 50
Table 4. Risk factors for type i and type ii dissociation.

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Type I NO (%)</th>
<th>Type II NO (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4(33.3)</td>
<td>5(50.0)</td>
<td>0.361</td>
</tr>
<tr>
<td>Female</td>
<td>8(66.7)</td>
<td>5(50.0)</td>
<td></td>
</tr>
<tr>
<td>Drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2NRTI+PI</td>
<td>2(16.7)</td>
<td>3(30.0)</td>
<td></td>
</tr>
<tr>
<td>2NRTI+NNRTI</td>
<td>4(33.3)</td>
<td>1(10.0)</td>
<td>0.400</td>
</tr>
<tr>
<td>NRTI+NNRTI+PI</td>
<td>6(50.0)</td>
<td>6(60.0)</td>
<td></td>
</tr>
<tr>
<td>Age (yrs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-44</td>
<td>8(66.7)</td>
<td>10(100.0)</td>
<td></td>
</tr>
<tr>
<td>45-64</td>
<td>4(33.3)</td>
<td>0(0)</td>
<td>0.046</td>
</tr>
<tr>
<td>BLCD4(cells/mm³)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;100</td>
<td>4(33.3)</td>
<td>7(70.0)</td>
<td></td>
</tr>
<tr>
<td>&gt;100</td>
<td>8(66.7)</td>
<td>3(30.0)</td>
<td>0.087</td>
</tr>
</tbody>
</table>

Results are presented as Means ± S.D. P value is significant at P < 0.05

Plate 1. Band of the amplified DNA with amplicon size of 500bp.
that were subjected to PCR. Lane 1 contains the DNA ladder or marker. This is the fermentsa 1kbp DNA ladder. Lane 2 is the negative control. Lanes 3 to 10 contain the DNA amplicons. Only sample 70 (Lane 5) was amplifiable and it gave a band size of 500 bp. The low amplification observed in this research is most likely to be associated with the variety in HIV-1 subtypes.

Discussion

The criteria for the classification of immunovirologic responses following HAART was adopted from Jevtovic et al. (2005) and WHO (2009). The response types include concordant responders with favorable response, concordant non responders with failure response, discordant responses namely; immunologic non responders (Type 1) dissociation and immununologic responders (Type 2) dissociation. The markers for response include CD4 count and viral load levels. The concordant responders are usually depicted as (VL+/CD4+) and this means that they show a highly improved CD4 response (>400cells/mm³) following therapy while their viral load has reduced to undetectable levels (<400copies/mL) for the Roche Amplicor system. For the concordant non responders (VL-/CD4-), their CD4 count fails to improve (<200cells/mm³), following HAART therapy and their viral load remains on the high level i.e. >5000copies/ml as stipulated by WHO for viral load levels used to define virologic failure. For the immunological non responders i.e. those with immunologic failure, (VL+ /CD4-), their CD4 count (<400cells/mm³) fails to get back to normal values i.e. greater than or equal to 400cells/mm³ despite undetectable viral load i.e. a good virologic response (Type I dissociation). Then, for the immununologic responders i.e. those with virologic failure (VL-/CD4+), their CD4 count appreciates beyond the level that may allow for opportunistic infections or AIDS defining illness i.e. greater than 200cells/mm³ but their viral load continues to be high (>5000cells/mm³) despite the immunological improvement and they are classified as Type II dissociation. While HAART allows for the reconstitution of immune functions in most treated HIV patients, discrepant responses including failure to achieve a significant increase in circulating CD4+ T cells despite undetectable plasma viral loads (pVL), or a good immunological response while not reaching undetectable viremia, may occur.

The various types of response to HAART, is shown (Table 1) and includes, favorable response (VL+/CD4+), failure (VL-/CD4-), and Type I (VL+/CD4-) and Type II (VL/CD4+) discordant responses. Fifty representative samples were used for this analysis. In all, 2(4%), showed a favorable response (VL+/CD4+), i.e. those who responded well to treatment (with CD4 count greater than 400 cells/mm³ and viral load undetectable i.e. ≤ 400copies/ml). However, 18(36%) failed on treatment with a mean CD4 count of 100.61±49 as against that of favorable response with a mean CD4 count of 675.00±348 and the difference is statistically significant at P < 0.05. The difference between the mean viral load of the favorable (400.00 ± 00) and failed (63643.50±62010) responses is not statistically significant with p > 0.05. The CD4 count and Viral load levels of 8(16%) subjects did not meet the criteria for classification as described above. This Table 1 shows that majority are failing on treatment. For the discordant responses, 12(24%) are experiencing immunological failure (Type I dissociation) with mean CD4 count of 162.42 ± 137 and favorable virological response with mean viral load count of 400.00 ± 00 copies per ml. Despite achieving an undetectable viral load, this group of patients fails to fully achieve immune reconstitution. Those with type II dissociation (10[20%]) fail to achieve reduced viral load levels despite ongoing immune reconstitution with mean CD4 count of 340.00 ± 190cells/ mm³ and viral load levels of 48320.40 ± 46387 copies/ml. The difference between the CD4 counts and viral load levels of both the Type I and Type II dissociation are significant with both having P -values less than 0.05. In a similar study, (Jevtovic et al., 2005), involving a series of 446 HIV patients, dissociative viro-immunological responses occurred in 50%, including 39% with a poor immunological response despite undetectable viremia (type 1 dissociation), and 11% with favorable immunological response but in the presence of detectable viremia (type 2 dissociation). Even though definitions of immunologic success vary between studies, individuals with discordant responses on HAART (‘virological only’, without an appropriate immunological response, or ‘immunologic only’ without viral suppression) consistently perform worse than individuals with complete responses (both virological and immunological), yet generally do better than those with no response. One observational, multicenter study found that after 4 years of follow-up, the rate of clinical disease progression was six-times greater in nonresponders, 1.9-times greater in virologic-only responders and 2.3-times greater in immunologic-only responders. However, patients with virologic-only response or with immunologic-only response had a significantly reduced risk for clinical progression than nonresponders (Nicastriti et al., 2005).

This study (Table 2) shows that having taken HAART for about 3 years and 2 months, more women 11(61.1%) than men 7(38.9%) failed on HAART therapy. Though, some other studies have affirmed that men do better on HAART than women. Rosin el al, (2014) in Switzerland, found that compared with men, women were less likely to achieve HIV RNA < 50 copies/mL at 1 year (75.2% versus 78.1% of men; P = 0.029) and at 2 years (77.5% versus 81.1%, respectively; P = 0.008). There were more women 8(66.7%) in the Type I dissociation response than men 4(33.3%). This shows that women are most likely to
be immunologically non responsive than men. This means that HIV infected women in the study environment may not increase their CD4 count greatly above the level for overcoming opportunistic infections even in the face of improved virologic outcomes. This could be associated with poor educational background, poor nutritional quality and other factors that make women more vulnerable to HIV/ AIDS especially in low income communities. Subjects with least baseline CD4 count 96.88±66 failed on HAART, achieving only marginal increase in HAART (100.61±49) after 3 years and 2 months on HAART. However, those with highest baseline CD4 count 225.50±35 had favorable response to HAART and achieved a geometric increase in CD4 count (675.00±347) after 3 years on HAART. This is consistent with the findings by Hrishikesh et al. (2015) in South Carolina that Individuals with CD4 count ≤200 cell/mm³ had significantly slower decrease in VL over time than those with CD4 count 201–350, 351–500, and >500 cell/mm³ (all p values <0.0001). Similarly, VL declines in individuals with CD4 counts 201-350 and 351-500 cell/mm³ were slower than for those with counts >500 cell/mm³ (p < 0.0001).

In addition, this study also shows that women with mean baseline CD4 count of 162.51±149 possibly initiated HAART treatment earlier in the course of infection than men with baseline CD4 count of 128.47±89. This is similar to the findings of Thorsteinsson et al. (2012). They found that women initiated HAART at higher CD4 counts (adjusted p = 0.026) and lower viral loads (adjusted p = 0.0003). However, men had better immunological response with current CD4 count of 248.68 ± 267 while on HAART than women with 190.03 ± 129.09. This low immunological response from women, despite starting HAART on a higher CD4 count than men could be due to confounding factors such as low educational background, poor nutritional quality, stigma and other predisposing factors associated with resource poor settings. Women, however, had lower current viral load 29424.54 ± 55497 than men 39163.68 ± 42616.

The risk factors associated with dissociative responses to highly active antiretroviral therapy are shown in Table 4. In the Type II dissociative response, men and women are equally represented, while women 8(66.7%) are more than men in the Type I response. The relationship between sex and Type I and II responses are not significant with P>0.05. In drug classification, there is no significant relationship between the type of drug the participant takes and the discordant response to that drug. However, those with Type II dissociation are mostly on Protease inhibitor combination i.e. 2NRTI + PI (3 [30%]) and NRTI+ NNRTI + PI (6 [60%]) with only 1(10%) taking the 2NRTI+NNRTI combination. The usage of PI-containing regimens was shown to be protective against a discordant response. The usage of PIs, modulates activation of peripheral blood CD4 cells and decreases their susceptibility to apoptosis (Sloand et al., 1999), this may explain prolonged survival of peripheral CD4 T cells even in the presence of continued viral replication (Type II dissociation). In contrast, NRTI usage could be associated with clinically relevant concentrations of dideoxynucleosides, which reduce cell growth by hampering DNA replication and inducing apoptosis (Viora et al., 1997). Given enough time, and favoring PI-based HAART regimens or those composed of three drug classes, patients with advanced immunodeficiency still have a chance to achieve favorable responses. This is in accordance with data from the EuroSIDA study (Piketty et al., 1998). Little is known about the mechanisms underlying the development of discordant responses, but it apparently is dependent on the interaction of a multitude of viral and host factors. One hypothesis is that HAART selects viral strains that are less fit, which, in turn, results in reduced pathogenicity of drug resistant viruses. In fact, it has been shown that recipients of PI based regimens with prolonged discordance (immunologic success despite virological failure) have decreased viral replication capacity (Deeks et al., 2001). Those with Type I and Type II responses predominate in the 25 - 44 age bracket with 8(66.7%) in the Type I group and 10(100%) in Type II. The age of an individual has a significant relationship with Type I and Type II responses with P<0.05. The baseline CD4 count was found to have no significant relationship with both the Type I and Type II dissociative responses with P>0.05. Type I response occurred more in individuals with baseline CD4 count more than 100cells/mm³ while the Type II response occurred more in individuals with baseline CD4 count less than 100cells/mm³.

In all, 50 different RNA extracts were subjected to PCR amplification reactions for possible drug resistance studies. Only one sample was amplified out of the 50 that were subjected to PCR. The low amplification observed in this research is most likely to be associated with the variety in HIV-1 subtypes in Nigeria. This amplification was performed to determine the potentials for drug resistance testing in our local environment. The primer sequence used in this study effectively amplified HIV strains found in Jos, Nigeria (Lar et al., 2007), but performed poorly with the strains found in Anambra State. This low amplification potential presents another challenge and prompts for development of primers that can effectively amplify the strains found in Southeast Nigeria. It has been reported (Njouom et al., 2003), that HIV subtype variety affects primer binding and hence, amplification potentials. There have been reports on a diverse array of subtypes including CRF02_AG, G, CRF06_cpx, A3, and unique recombinant forms that appear to differ geographically within Nigeria (Sankale et al., 2007). Similar distributions of HIV-1 subtypes have also been described in other West African countries including Senegal (Hamel et al., 2007), Cameroon
(Brennan et al., 2008), Ivory Coast (Ellenberger et al., 1999), and Gambia (Cham et al., 2000). Until recently, antiretroviral drugs were developed and tested for efficacy with subtype B viruses as the reference. The clinical effectiveness of these drugs and their patterns of drug resistance were established in clinical trials conducted for the most part on patients infected with subtype B. Although, most drugs would be expected to act on targets that were conserved as a result of their critical function in the viral replication cycle such as reverse transcription, protein processing (protease), integration, and co-receptor binding, it seems probable that genetic differences between subtypes might impact the drug resistance pathways or kinetics of drug resistance development (Ode et al., 2007).

Conflict of interest

The authors declare that there is no conflict of interest.

Funding

The funding for this research was from personal sources.

Research constraints

The unavailability of funding was a major drawback in this research. The sample size had to be reduced due to unavailability of research grant.

REFERENCES


