Journal of Advances in Medicine and Medical Research

32(3): 98-105, 2020; Article no.JAMMR.55396
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

Factors Influencing Viral Load Non-suppression among People Living with HIV (PLHIV) in Borno State, Nigeria: A Case of Umaru Shehu Ultra-Modern Hospital

Fadoju Sunkanmi[1*], Yunana Paul[1], Dickson Peter[1], Affiah Nsikan[1], Jasini Joseph[1], Emmanuel Opada[1], Udenenwu Henry[1], John Jonah[1], Kyeshir Tapshak[1] and Ndifreke James[1]

[1]Achieving Health Nigeria Initiative, FHI 360, Global Fund - Impact HIV Project, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. Author FS came up with the idea for the study, took part in the collection of data, analysis for the study and participated in writing of the first draft of the manuscript. Author YP led the team members of the global fund project. All authors took part in the data collection process, analysis of the study, discussions and writing of the abstract. All authors also read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2020/v32i330388
Editor(s):
(1) Dr. Rameshwari Thakur, Muzaffarnagar Medical College, India.
Reviewers:
(1) Moukaila Abdou Razak, University of Lome, Togo.
(2) Bora Ekinci, Mugla Sitki Kocman University, Turkey.
Complete Peer review History: http://www.sdiarticle4.com/review-history/55396

Original Research Article

Received 09 January 2020
Accepted 13 March 2020
Published 21 March 2020

ABSTRACT

Background: The 2019 National AIDS Indicator and Impact Survey (NAIIS) report showed that the prevalence of HIV in North East Nigeria is 1.1%. Despite the increasing number of patients on ART in Nigeria, there is inadequate information about clients with virologic failure and its different determinants among PLHIVs enrolled into care in resource-limited and security challenged settings like Borno state.
Objectives: To evaluate the suppression rate and the associated factors for non-suppression of Viral Load (VL) at a HIV/AIDS comprehensive service delivery site in Borno State.
Methods: A case study conducted using routinely received Viral Load (VL) test results in Umaru Shehu Ultra-Modern Hospital, Borno State. Six (6) VL data from 402 patients on HIV anti-retroviral

**Corresponding author: E-mail: sunkanmi.fadoju@gmail.com;*

therapy (ART). Data collected using standard tools and Lafiya Information Management System (LAMIS) used for data extraction and STATA 14 used for analysis. Logistic regression was employed to identify various factors associated with viral Load non-suppression (virologic failure) in the selected facility in the State.

Results: From the 402 patients; 279 (69.40%) were females while the remaining 123(30.60%) were males. Overall virologic failure/non-suppression rate was 16.33%. 19.2% of the patients age 25-29 were virally unsuppressed. The odds of virologic failure decreased with age, with children aged 5-9 years (OR= 1.97, 95%CI = 0.02-169.913) and adults (OR= 3.33, 95%CI = 0.064-171.66) registering the highest odds. Last clinical stage (OR= 1.54, 95%CI = 0.499-4.76) and Body mass Index (OR= 1.4, 95%CI = 0.5-4.33) increased the odds of virologic failure.

Conclusions: Demographic, economic and clinical data study increased the odds of virologic failure. Second line and third line ART regimens were protective against virologic failure. The study recommends close monitoring and regular follow up on patients by the case managers/care givers/treatment supporter and intensified patients' adherence support for repeat testers after suspected failure of the drug.

Keywords: Antiretroviral; HIV; suppression; viral load.

1. INTRODUCTION

Antiretroviral therapy (ART) has changed the natural history of HIV infection [1]. By the end of 2015 about 36.7 million individuals were living with HIV globally and 25.8 million of these were living in sub-Saharan Africa (SSA) [2,3]. By June 2016, ART coverage had increased to 46% globally and 54% in SSA [2].

Access to antiretroviral therapy (ART) has continued to improve in recent years, however there is still concern that not all patients that need ART will have access to it due to the rising number of infected HIV patients. Thus, to sustain the success recorded in ART availability to patients and limit development of treatment failure, WHO in July 2013 recommended viral load testing as the approved monitoring approach to diagnose treatment failure [4,5]. Monitoring viral suppression among patients enrolled on ART is important for timely detection of treatment failures, identification of patients in need of more intensive adherence support and minimizes development of drug resistance and unnecessary switch to expensive and limited ART regimen options [6,7].

Previous studies have highlighted several factors that may be associated with viral suppression. Patients with WHO clinical staging 4 are more likely to be virally non-suppressed while those whose health status is evaluated by physicians on each clinic visit are less likely to experience virologic failure [8]. Children and adolescents on ART are more likely to have high viral loads [9]. Suboptimal adherence, poor tolerability, and drug and food interactions, CD4 cell count, treatment history and drug-resistance (primary or transmitted) have also been associated with virologic failure. Suboptimal adherence and drug intolerance are the major cause of regimen discontinuations and virologic failure [10,11,12]. Virologic failure may also be caused by patient-related factors such as co-morbidities, incomplete medication adherence, missed clinic appointment and interruption of or intermittent access to ART, and ARV regimen related factors such as drug adverse effects, suboptimal pharmacokinetics, suboptimal HIV anti-retroviral agent and food requirements, amongst other factors [13].

ART initiation reduces HIV replication in peripheral blood [14-18] suppresses plasma HIV viral loads (VL) to unquantifiable levels within 4-6 months [19,20], reduces morbidity and mortality, with resultant improvement in survival [1,5]. If adequate viral suppression is not achieved, therapy is failing and may require switching to a second line ART regimen [21,22] which may be both expensive and toxic.

HIV RNA virological monitoring is the gold standard for measuring ART progress [23-29]. Although HIV viral suppression requires good ART adherence in excess of 95% [30], suboptimal viral suppression due to poor adherence has undermined HIV care in SSA since introduction of free ART programmes in 2004-2005. Many other factors are independently associated with failure to achieve optimal HIV viral suppression [28]. Knowledge of such predictors will enable clinicians forecast ART outcomes and design interventions to prevent virologic failure and meet the UNAIDS 90- 90-90

treatment targets. Diagnosis of virologic failure based on a single plasma VL measurement of > 1000 copies/ml or two successive VL measurements above 400 copies/ml, at any time after 6 months on ART, (conventional VL), has led to unnecessary switching from first to second line ART regimen which is costly and almost currently the last available treatment option in most SSA countries [31]. If patients with detectable VL after 6 months on ART receive further intensified ART adherence counselling and continue first-line ART for another 6 months, only those whose VL remains >1000 copies/ml (true or pragmatic virological failure) are then switched to second-line ART.

The 2019 NAIIS report showed that the prevalence of HIV in North East Nigeria is 1.1%. Despite the increasing number of patients on ART in Nigeria, there is inadequate information about virally unsuppressed clients and its different determinants among PLHIVs enrolled into care in resource-limited and security challenged settings like Borno state. This study evaluated the suppression rate and the associated factors for non-suppression at a Global Fund (GF) supported site in Borno state.

2. MATERIALS AND METHODS

2.1 Description of Study Area

A case study was conducted in Dikwa, Bama (Banki) and Ngala LGAs of Borno State, Nigeria. Ngala, Dikwa and Bama LGAs have an estimated area of 1,465 km² 1,774 km² and 4,997 km^2 respectively. The population of Ngala, Dikwa and Bama (Banki) LGAs based on 2006 census was 237,071 persons, 25,300 persons and 269,986 persons respectively. However, the population dynamics has changed over time attributed to population growth, population movement/ displacements as result of insurgency and thus population from 2006 census may not be the current population of the mentioned LGAs. The HIV prevalence rate in Borno state was pegged at 1.1% (NAIIS, 2019).

2.2 Study Design

A case study was conducted using routinely received VL test results in Umaru Shehu Ultra-Modern Hospital (USUMH), Maiduguri Borno State.

2.3 Sampling Frame

Data from January 2019 to June 2019 were pulled from patient records through Lafiya Management information System (LAMIS) software. From the Clients Care Cards, we obtained demographic, economic and clinical data.

2.4 Sample Size

VL data for 402 patients on ART for 6 months was analyzed and used. Variables in the Clients Care Cards were compared using chi-square test.

2.5 Method of Data Collection

Data were routinely collected on patients' viral loads using standard tools like the viral load testing register, ART client care cards in the selected 3 IDP camps in Borno State. Data was also collected based on patients on 1st line ART regiment (generally an association of 2 nucleosides inhibitors of reverse transcriptase+ 1 Non-Nucleoside inhibitor of reverse transcriptase, 2nd line (2 nucleosides inhibitors of reverse transcriptase+ 1 Protease inhibitors), 3rd line and 4th line regiments.

2.6 Method of Data Analysis

Statistical tests were two-sided and P-value < 0.5% was considered statistically significant. The STATA 14 statistical software was used for all analyses. However, logistic regression was employed to identify various factors associated with viral non-suppression in the selected facility in the State.

2.7 Inclusion Criteria

Patients of all ages attending ART clinic were screened for HIV.

3. RESULTS

Patients' characteristics- [Proportion of patients with virological non-suppression].

Table 1 shows the characteristics of the 402 clients whose viral load data were available for analysis. Of the 402, 334 achieved virologic suppression, 68 were virally un-suppression.

From the table, Age in groups and Marital status significantly affect viral load unsupression. However, patients in the age group 25-29 years were found to achieve virologic failure. Also, from the patients' marital status, 58.73% of the married patients were found to achieve virologic failure.

Table 2 depict the clinical factor of patients whose viral load data were available for analysis. Variables such as current regimen, viral load type, BMI and clinical stage were considered. Of these patients, 39 (15.8%) with viral load greater than 1000 copies/ml were presently on TDF-3TC-EFV. Also, larger proportion 65 (100%) were repeaters with low BMI, were in the clinical stage1 and 36 (16.4%) with viral load >1000 copies/ml respectively.

Table 1. Socio-demographic profile of patients and viral load, January 2019 to May 2019 (n = 402)

Socio demographic variables	Viral load (n=402)	
	<1000 copies/ml n(%)=334	>1000 copies/ml n (%)=68
Age in groups ***		
0-4	3 (37.50)	5 (62.50)
5-9	2 (50.0)	2 (50.0)
10-14	2 (50.0)	2 (50.0)
15-19	22 (71.43)	4 (28.57)
20-24	40 (80.0)	10 (20.0)
25-29	124 (80.76)	30 (19.24)
30-34	63 (81.82)	8 (18.18)
35+	78 (89.74)	8 (10.26)
Sex		
Male	99 (82.5)	21 (17.5)
Female	235 (84.84)	42 (15.16)
Marital Status ***		
Single	260 (93.53)	18 (6.47)
Married	26 (41.27)	37 (58.73)
Widowed	27 (81.82)	6 (18.18)
Separated/Divorce	3 (100.0)	0 (0.0)
Educational Qualification		
No Education	60 (58.89)	44 (42.11)
Primary Education	40 (80.0)	10 (20.0)
Secondary Education	39 (93.0)	3 (7.0)
Post -Secondary	32 (78.05)	9 (21.95)

**** Depict the p-value (p=0.05)*

Table 2. Clinical factors of patients and viral load, January 2019 to May 2019 (n = 402)

Clinical variables	Viral load *n=402*	
	<1000 copies/ml n(%)=334	>1000 copies/ml n(%)=68
Current regimen		
1st Line	41 (70.69)	17 (29.31)
2nd line	66 (85.71)	11 (14.29)
3rd Line	213 (84.52)	39 (15.48)
Viral load type ***		
Baseline	28 (90.32)	3 (9.68)
Repeat	0 (0.9)	65 (100.0)
Routine	20 (100.0)	0 (0.0)
Second	286 (100.0)	0 (0.0)
Body mass index ***		
Low BMI	0 (0.0)	3 (100.0)
High BMI	3 (75.0)	1 (25.0)
Clinical stage		
Stage I	187 (83.86)	36 (16.14)
Stage II	96 (84.21)	18 (15.79)
Stage III	51 (79.69)	13 (20.31)
Stage IV	0 (0.0)	1(100.0)

**** Depict the p-value (p<=0.05)*

Table 3. Factors associated with virologic failure among HIV patients on ART, January 2019 to May 2019

Associated factors	Odd ratio	Std. Err.	z	p>|z|	95% CI	
Patient's factors					**Lower**	**Upper**
Age group						
0-4	1.0000(RC)					
5-9	1.973331	.119048	-0.13	0.898	.0211431	169.913
10-14	2.107243	1.353545	-3.51	0.037	.0301823	21.5902
15-19	2.2230651	.3148782	-1.06	0.288	.0140242	3.548019
20-24	2.2807102	.2807615	-1.27	0.204	.0395277	1.993495
25-29	3.1148053	.114563	-2.17	0.030	.0162388	.8116481
30-34	3.2547054	.2670432	-1.30	0.192	.0326291	1.988253
35+	3.33	.1526103	-1.91	0.056	0.064	171.66
Sex						
Male	1.0000(RC)					
Female	.9756625	.4731366	-0.05	0.959	.3771542	2.523947
Marital status						
Single	1.0000(RC)					
Married	.0507513	.0675689	-2.24	0.025	.0037341	.6897838
Widowed	.1620115	.2269677	-1.30	0.194	.0104008	2.523622
Separated/Divorce	.1412284	.1990035	-1.39	0.165	.0089228	2.23533
Educational qualification						
No Education	1.0000(RC)					
Primary Education	1.274031	1.459008	-3.66	0.566	0.869553	1.54462
Secondary Education	1.76384	1.957904	-1.92	0.431	0.722780	1.854978
Post -Secondary	13.43713	15.811731	-1.42	0.726	1.043089	5.50233
Clinical factors						
Current regimen						
1st line	1.0000(RC)					
2nd / 3rd line	9.042118	0.806836	-2.54	0.00	0.22	36.594
Viral load type						
Baseline	1.0000(RC)					
Repeat	2.6716	0.5322	-0.51	0.355	1.8080	3.9477
Routine	2.4000	0.4716	-2.11	0.000	1.6329	3.5276
Second	2.1021	0.5892	-2.44	0.223	1.7624	4.1430
Body mass index						
Low BMI	1.0000(RC)					
High BMI	1.4221	1.6336	-2.71	0.133	0.5211	4.3302
Clinical stage						
Stage I	1.0000(RC)					
Stage II	1.4288	0.6866	-3.22	0.002	1.3956	4.2270
Stage III	1.4626	0.9123	-1.43	0.000	2.0660	5.8033
Stage IV	1.5411	0.1096	-1.82	0.066	0.4990	4.7625

*Note: Number of observation = 402, Likelihood ratio chi-square = 27.89, Degree of freedom = 401, p-value=0.022*** *RC = Reference category*

Table 3 shows the odds ratios associated with virologic failure by reason of viral load testing and other background characteristics. At multivariate analysis level. the odds of virologic failure increased with age, in children aged 5-9 years (OR= 1.97, 95%CI = 0.02-169.913) and adults (OR= 3.33, 95%CI = 0.064-171.66) registering the highest odds. Virologic failure is higher among repeat testers, Last clinical stage (OR = 1.54, 95%CI = 0.499-4.76) and Body mass Index (OR = 1.4, 95%CI = 0.5-4.33) increased the odds of virologic failure. However,

being on second/third line regimens (OR= 9.04, 95%CI = 0.22-0364.59) protected patients against virologic failure.

4. DISCUSSION

This case study was conducted to estimate the proportion of patients with virologic failure and to identify the factors associated with virologic failure (an overall proportion of 16.33%). Amongst the patients, repeat tester after suspected treatment failure, young age, clinical stage increased the odds of virologic failure. Being on second/ third line regimens protected patients against virologic failure. The study revealed that the overall proportion of virally non-suppressed patients were lower in number compared to suppressed patients (i.e. 68 non suppressed out of 402 patients), this is surprisingly comparable to the repeat testers (received VL retesting after Initial suspected failure registered) who recorded the highest virologic failure among the patients. This could be because repeat testers after suspected failure pending confirmation, are more likely not to adhere to their medicines and therefore being at highest risk for virologic failure compared to other patients' group in the study.

Although the Nigeria viral load monitoring guidelines recommend strict adherence counseling and support for patients whose first VL result is far greater than 1000 copies/ml, the study was unable to determine if the program is giving enough attention to these patients as this was not considered in this study. Albeit, it is important to ensure that all patients who were virologically non-suppressed during first VL testing be retested again after a period of adherence to ART. Hence, building more efficient mechanisms for effective follow-up and consistent monitoring of patients on antiretroviral treatment to prevent virologic failure is important. High VL non-suppression was also recorded among married patients (58.73%) compared to singles patients. The reason for this could not be determined however this is a possible area of research.

The results also showed that children and young adolescents were more likely to experience virologic failure compared to the rest of the age groups. This finding corroborates the report of a recent study conducted in the US that older patients were more likely to achieve viral suppression [32]. The reasons for this could be because, treatment for children and adolescents presents numerous difficulties which includes; the intricacy in ARV medication and the need to adjust doses as the children grow, which may not be easy especially for clinicians who are not skilled enough with pediatric care or too busy to track the suppression status of those children. Also, Stigma, fear of disclosure, and stress may affect younger people more than their older counterparts [33].

Finally, from the results, treatment failure was high among married women, patients on first lie regiment and repeat testers. This cuts across both sociodemographic and clinical factors confirming that these factors do influence viral load non suppression among People Living with HIV (PLHIV).

5. CONCLUSION AND RECOMMENDATION

The demographic, economic and clinical data employed for this study increased the odds of virologic failure while second/third line ART regimens were protective against virologic failure. The study recommends close monitoring of patients and regular follow up on patients by the case managers and intensified patients' adherence support for repeat testers after suspected failure of the drug. Counselling should also focus on encouraging spouses of married patients to act as treatment supported for their partners.

6. MAJOR LIMITATION

Incomplete patient's records pose a challenge for this study. However, in order to guarantee quality data, the laboratory services unit closed this gap by making immediate phone calls and adequate follow-up to health facilities where the samples were derived.

CONSENT

Consent was obtained from all clients using the client intake form. This is a standard tool that has been approved by the Federal Ministry of Health for use in all HIV Counselling and Testing Services. Consent was also obtained from Umaru Shehu Ultramodern Hospital Ethical Committee.

ETHICAL APPROVAL

Ethical approval was given by the Hospital's Ethics committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Palella Jr. FJ, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. New England Journal of Medicine. 1998; 338(13):853- 60.
2. UNAIDS. How AIDS changed everything; 2016.
(Accessed on 26 November 2016)
3. UNAIDS. The HIV and AIDS Uganda Country Progress Report; 2014.
(Accessed on 6 October 2015)
4. WHO. Antiretroviral Therapy (ART) coverage among all age groups; 2015.
[Cited on 2017 20/03/2017]
Available:from: http://www.who.int/gho/hiv/epidemic_response/ART_text/en/
5. WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, recommendations for a public health approach. 2013
[Cited on 2016 01/10/2016]
Available:http://www.who.int/hiv/pub/arv/arv-2016/en/
6. WHO. World Health Organization. HIV drug resistance; 2006.
[Cited on 2016 02/03/2016]
Available:http://www.who.int/hiv/topics/drugresistance/en/
7. WHO. Technical Brief on HIV Viral Load Technologies; 2010
[Cited on 2015 20/10/2015]
Available:http://www.who.int/hiv/topics/treatment/tech_brief_20100601_en.pdf
8. Huong DTM, Bannister W, Phong PT, Kirk O, Peters L. Factors associated with HIV-1 virological failure in an outpatient clinic for HIV-infected people in Haiphong, Vietnam. Int J STD AIDS. 2011;22(11):659–64.
9. Jobanputra K, Parker LA, Azih C, Okello V, Maphalala G, Kershberger B, et al. Factors associated with virological failure and suppression after enhanced adherence counselling, in children, adolescents and adults on antiretroviral therapy for HIV in Swaziland. PLoS One. 2015;10(2):–e0116144.
10. d'Arminio Monforte A, Lepri AC, Rezza G, Pezzotti P, Antinori A, Phillips AN, et al. Insights into the reasons for discontinuation of the first Highly Active Antiretroviral Therapy (HAART) regimen in a cohort of antiretroviral naive patients. I.CO.N.A. Study Group. Italian Cohort of Antiretroviral-Naive Patients. AIDS (London, England). 2000;14(5):499–507.
11. Mocroft A, Youle M, Moore A, Sabin CA, Madge S, Lepri AC, et al. Reasons for modification and discontinuation of antiretrovirals: Results from a single treatment centre. AIDS (London, England). 2001;15(2):185–94.
12. Paredes R, Lalama CM, Ribaudo HJ, Schackman BR, Shikuma C, Giguel F, et al. Pre-existing minority drug-resistant HIV-1 variants, adherence and risk of antiretroviral treatment failure. J Infect Dis. 2010;201 (5):662–71.
13. AIDSInfor. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Management of the Treatment-Experienced Patient; 2015.
14. UNAIDS. 90–90-90, An ambitious treatment target to help end the AIDS epidemic; 2014.
15. Hogg RS, Yip B, Kully C, Craib KJ, O'shaughnessy MV, Schechter MT. Improved survival among HIV-infected patients after initiation of triple-drug antiretroviral regimens. Canadian Medical Association Journal. 1999; 160(5):659-65.
16. Hirschel B, Opravil M. The year in review: antiretroviral treatment. AIDS (London, England). 1999;13SupplA:S177-87.
17. Notermans DW, Jurriaans S, de Wolf F, Foudraine NA, de Jong JJ, Cavert W. Decrease of HIV-1 RNA levels in lymphoid tissue and peripheral blood during treatment with ritonavir, lamivudine and zidovudine. Aids. 1998;12(2):167-73.
18. Gulick RM, Mellors JW, Havlir D, Eron JJ, Gonzalez C, McMahon D. Treatment with indinavir, zidovudine and lamivudine in adults with human immunodeficiency virus infection and prior antiretroviral therapy. New England Journal of Medicine. 1997; 337(11):734-9.
19. Dybul M, Fauci AS, Bartlett JG, Kaplan JE, Pau AK. Guidelines for using antiretroviral agents among HIV-infected adults and adolescents. Annals of internal Medicine. 2002;137(5 Pt 2):381-433.
20. Carpenter CC, Cooper DA, Fischl MA, Gatell JM, Gazzard BG, Hammer SM. Antiretroviral therapy in adults: Updated recommendations of the International

AIDS Society? USA Panel. Jama. 2000;283(3): 381-90.
21. Flexner C. HIV-protease inhibitors. New England Journal of Medicine. 1998; 338(18):1281-93.
22. DeGruttola V, Dix L, D'Aquila R, Holder D, Phillips A, Ait-Khaled M. The relation between baseline HIV drug resistance and response to antiretroviral therapy: Re-analysis of retrospective and prospective studies using a standardized data analysis plan. Antiviral therapy. 2000;5(1):41-8.
23. Ministry of Health Uganda. Addendum to the National Antiretroviral Treatment Guidelines for Uganda. 2013. Accessed on 3 February 2017. 14. Katzenstein DA, Hammer SM, Hughes MD, Gundacker H, Jackson JB, Fiscus S. The relation of virologic and immunologic markers to clinical outcomes after nucleoside therapy in HIVinfected adults with 200 to 500 CD4 cells per cubic millimeter. New England Journal of Medicine. 1996;335(15):1091-8.
24. Kaufmann GR, Perrin L, Pantaleo G, Opravil M, Furrer H, Telenti A. CD4 T-lymphocyte recovery in individuals with advanced HIV-1 infection receiving potent antiretroviral therapy for 4 years: The Swiss HIV Cohort Study. Archives of internal medicine. 2003;163(18): 2187-95. PubMed | Google Scholar.
25. Moore RD, Keruly JC, Gebo KA, Lucas GM. An improvement in virologic response to highly active antiretroviral therapy in clinical practice from 1996 through 2002. JAIDS Journal of Acquired Immune Deficiency Syndromes. 2005;39(2):195-8. PubMed | Google Scholar.
26. Powderly WG, Saag MS, Chapman S, Yu G, Quart B, Clendeninn NJ. Predictors of optimal virological response to potent antiretroviral therapy. Aids. 1999;13(14): 1873- 80. PubMed | Google Scholar.
27. Mellors JW, Rinaldo Jr. CR, Gupta P, White RM. Prognosis in HIV-1 infection predicted by the quantity of virus in plasma. Science. 1996;272(5265):1167. PubMed | Google Scholar.
28. O'brien WA, Hartigan PM, Martin D, Esinhart J, Hill A, Benoit S et al. Changes in plasma HIV-1 RNA and CD4+ lymphocyte counts and the risk of progression to AIDS. New England Journal of Medicine. 1996; 334(7):426-31. PubMed | Google Scholar.
29. Piacenti FJ. An update and review of antiretroviral therapy. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2006;26(8):1111-33.
PubMed | Google Scholar
30. Deeks SG. Determinants of virological response to antiretroviral therapy: Implications for long-term strategies. Clinical Infectious Diseases. 2000; 30(Supplement 2):S177-S84. PubMed | Google Scholar.
31. Keiser O, Tweya H, Boulle A, Braitstein P, Schechter M, Brinkhof MW, et al. Switching to second-line antiretroviral therapy in resource-limited settings: comparison of programmes with and without viral load monitoring. AIDS (London, England). 2009; 23(14):1867. PubMed | Google Scholar.
32. Yehia BR, Rebeiro P, Althoff KN, Agwu AL, Horberg MA, Samji H, et al. The Impact of Age on Retention in Care and Viral Suppression. J Acquir Immune Defic Syndr. 2015;68(4):413–9.
33. Katz IT, Ryu AE, Onuegbu AG, Psaros C, Weiser SD, Bangsberg DR, et al. Impact of HIV-related stigma on treatment adherence: systematic review and meta-synthesis. J Int AIDS Soc. 2013;16(3 Suppl 2):18640.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/55396