Relationship of Smoking with the CD4+ T cell count and Viral Load in Patients with the Human Immunodeficiency Virus in the HIV health care center at the Hospital Regional Universitario José María Cabral y Báez in the Dominican Republic: a Cross-sectional Descriptive Study

Anneris Estevez[1,2,*], Guillermo Andrés Taveras Soriano[1,3], Adalberto Rodríguez Velazquez[1,4], Sergio Díaz[1,5,6,7], Zahira Quiñones de Monegro[1,5,8], José Javier Sánchez[1,5,9]

Abstract

Objective: To evaluate the relationship between tobacco use and viral load and CD4+ T cell count in HIV patients.

Results: The research conducted was a descriptive study of 317 patients on highly active antiretroviral therapy (HAART), 18 years old and above, who attended the "Unidad de Atención Integral" (UAI) at the Hospital Regional Universitario José María Cabral y Báez, in Santiago, Dominican Republic. Of those 317 patients, 172 were included in the data analysis. It was found that a 77.3% of smokers had a CD4+ T cell count equal to or below 250 cells/mm3. 75% of smokers had a viral load equal to or greater than 400 copies/ml. In addition, 82.9% of nonsmokers presented with a viral load below 400 copies/ml. The smokers were more likely to have a viral load equal to or greater than 400 copies/ml (OR = 6.285, P < 0.001), in comparison with nonsmokers. Patients younger than 45 years old were more likely to have a viral load equal to or above 400 copies/ml compared to older patients (OR = 3.313, P = 0.024).

Keywords: smoking, antiretroviral therapy, human immunodeficiency virus

Relación entre tabaquismo, conteo de CD4+ y carga viral en pacientes con infección por Virus de Inmunodeficiencia Humana en el centro de atención para VIH del Hospital Regional Universitario José María Cabral y Báez de Republica Dominicana: estudio descriptivo transversal

Resumen

Objetivo: Evaluar la relación entre el consumo de tabaco, la carga viral y el recuento de linfocitos T CD4+ en pacientes con VIH.

Resultados: La investigación fue realizada mediante un estudio descriptivo a 317 pacientes en terapia antirretroviral de alta actividad (TARGA), de 18 años o mayores, que asistían a la Unidad de Atención Integral (UAI) del Hospital Regional Universitario José María Cabral y Báez, en Santiago, República Dominicana. De esos 317 pacientes, 172 se incluyeron en el análisis de datos. Se encontró que un 77,3% de los fumadores tenían un recuento de células T CD4 + igual o inferior a 250 células / mm3. El 75% de los fumadores tenían una carga viral igual o superior a 400 copias / ml. Además, el 82,9% de los no fumadores presentaba una carga viral inferior a 400 copias / ml. Los fumadores tenían más probabilidades de tener una carga viral igual o superior a 400 copias / ml (OR = 6.285, P <0.001), en comparación con los no fumadores. Los pacientes menores de 45 años tenían más probabilidades de tener una carga viral igual o superior a 400 copias / ml en comparación con los pacientes mayores (OR = 3,313, P = 0,024).

Palabras claves: Tabaquismo, Terapia Antirretroviral, Virus de Inmunodeficiencia Humana

---

1 M.D., Medicine School, Faculty of Health Sciences, Pontificia Universidad Católica Madre y Maestra, Santiago, Dominican Republic
2 https://orcid.org/0000-0003-1938-0923
3 https://orcid.org/0000-0002-0342-0305
4 https://orcid.org/0000-0001-9846-4863
5 Hospital Metropolitano de Santiago (HOMS), Dominican Republic
6 Proyect Double T, Dominican Republic
7 https://orcid.org/0000-0003-0896-2792
8 https://orcid.org/0000-0002-4852-8897
9 https://orcid.org/ 0000-0002-6638-177X
* Autor para correspondencia.
   Correo electrónico: mellizas@comcast.net (AE)

Introduction

By decreasing the immune system's functional capacity, Human Immunodeficiency Virus (HIV) has become one of the greatest problems for the healthcare system, contributing significantly to the morbidity and mortality of HIV infected patients[1]. It is estimated that around 36.9 million people were living with HIV globally in the year 2017[2].

In the general population, tobacco use is one of the most important factors that reduce life expectancy and one of the most modifiable[3]. There is high prevalence of tobacco use in HIV patients, leading to an increase in the production of inflammatory cells, a greater viral replication and, in general, contribute to alterations capable of affecting the health of these patients[4,5]. Diverse problems exist, such as: a worse immunological response, as well as viral response; clinical manifestations induced by HIV; greater consumption of marijuana and alcohol; a decrease in quality of life; and greater risk of mortality[4].

Antiretroviral therapy, highly active antiretroviral therapy (HAART) has played a vital role in the reduction of viral replication[6]. The Dominican Republic is a country of great interest for future research. According to a progress report published by the World Health Organization (WHO), the island shared by the Dominican Republic and Haiti makes up about 70% of the cases of HIV in the Caribbean[7]. On its own, the Dominican Republic makes up 0.7% of the cases of HIV, covering 80% of the antiretroviral treatment costs for their population[8]. This country has been one of the primary tobacco producers in Latin America[9].

The objective of this investigation was to evaluate the relationship between the use of tobacco and the viral load and CD4+ T cell count in HIV patients in one of the "Unidad de Atención Integral (UAI)" sites, which are HIV health care centers, found in the Hospital Regional Universitario José María Cabral y Báez (the regional hospital of Santiago, Dom. Rep.). Patients were categorized as smokers, ex-smokers, and nonsmokers. The second objective was to create a logistic regression analysis to determine variables, such as tobacco use, age, sex, duration under antiretroviral treatment, length of time with diagnosis, depression and anxiety, illicit drug use, excessive alcohol consumption, sexually transmitted disease, and adverse reactions to treatment that may influence the effectiveness of the treatment.

Methods

A descriptive observational study was implemented. The population studied consisted of HIV patients 18 years old and above, on HAART antiretroviral therapy[3,10], who attended the UAI in the Hospital Regional Universitario José María Cabral y Báez in Santiago, Dominican Republic. The sample was selected from the total population, obtained from the monthly reports to the "Dirección Provincial de Salud de Santiago" (Provincial Health Directorate of Santiago), that were actively enrolled and had records in this HIV health care center[11,12].

Using a confidence interval of 95%, the sample size was from the reference population using Raosoft[13,14,15]. The sample size was 317 patients from a total of 1,789 patients enrolled at the UAI of which 172 patients met all of the following inclusion criteria: 18 years old or older; HIV diagnosis; on HAART; treatment adherence; be enrolled and have records at the UAI; and completed the informed consent. We screened the adherence to treatment as an inclusion criteria using the following approach from Friedman et al[11]: individuals were classified as "non-adherent" if they had missed taking at least one pill and "adherent" not having missed taking any pills during the two days prior to survey administration.

The study protocol and data accessed was approved by the Bioethics Committee, "Comité de Bioética de la Facultad de Ciencias de la Salud (COBE-FACS)", from the Pontifícia Universidad Católica Madre y Maestra. We worked with the medical doctors and personnel at the center, and as patients walked in, they would be approached and informed of the study and invited to participate voluntarily[16]. The CD4+ T cell count and viral load was obtained from their records and incorporated into the questionnaire[10,17].

The data was compiled using Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) program[18]. The variables that were taken into account in this study were all converted to qualitative dichotomous variables. The patients were categorized as smokers, ex-smokers, and never smokers using questions modified by the "Unidad Técnico Asesora de Investigación" (Investigation Department) of the Pontificia Universidad Católica Madre y Maestra taken from "Encuesta Mundial de Tabaquismo en Adultos" (Global Questionnaire for Tobacco Use in Adults)[19,20,21]. The use of tobacco was measured as the use of any tobacco product at least once a week[3].

Sex was either male or female[20]. The age was reported by the patients and was later classified into two groups: < 45 years old and ≥ 45 years old[1,22]. The greater the CD4+ T cell count (>250 cells/mm³) the greater the effectiveness of the treatment; likewise, the lower the viral load (<400 copies/ml), the more effective the antiretroviral treatment[6,23,24]. Depression and anxiety grouped into "Yes" (presence of a relevant clinical problem) and "No"[14]. Illicit drug use into "Yes" and "No" using questions 11, 12 and 13 from the Spanish version of the questionnaire provided by the New York State Department of Health, Bureau of Communicable Disease Control[13], specifically injected drugs, non-injected and/or inhaled drugs,[13] and a "Yes" to any one of these three questions classified the patient as a drug consumer.

Using the Center for Disease and Control's (CDC) parameters, excessive alcohol consumption was either "Yes", drinking 5 or more alcoholic beverages in one sitting for men and 4 or more alcoholic beverages for women in one sitting in the past 30 days[25], and "No". Adverse reaction took into account the most common adverse reaction(s) to the antiretroviral treatment reported in the pilot study, (dizziness, vomiting, night terrors and allergies).

The variables "duration under antiretroviral treatment" and "length of time with diagnosis" were reported as nominal polytomous variables and then converted into categorical dichotomous variables falling into the following: one year or more or less than one year[26]. History of sexually transmitted disease was divided into: having two or more sexually transmitted diseases, such as syphilis, chlamydia, gonorrhea, hepatitis A, B and/or C and the other was having only one sexually transmitted disease (i.e. HIV)[13].

Results

Approximately 60% of the participants were less than 45 years old; around 58.7% of the patients were female. 45.3% of the patients were categorized as current smokers. Those that were not classified as current smokers were further classified as either ex-smokers or never smokers, of which 17% were ex-smokers and 83% were never smokers. 21% of the patients analyzed had a viral load greater than or equal to 400 copies/ml; 13% had a CD4+ T cell count less than or equal to 250cells/mm^3.

Table 1 shows that 77.3% of patients with a CD4+ T cell count ≤ 250 cells/mm^3 were smokers. In regards to non-current smokers, 59.3% of patients with a CD4+ T cell count ≥ 251 cells/mm^3 were of this category (P = 0.001). In Table 2, 75% of patients with a viral load ≥ 400 copies/ml were smokers. 76 out of the 85 non-current smokers had a viral load ≤ 400 copies/ml (P < 0.001). No relationship was found between viral load and whether a patient was an ex-smoker or never smoker (P = 0.703). Figure 1 demonstrates the logistic regression analysis that was done with the viral load and all the variables included in the study. Controlling for the confounding variables, it was observed that the variables that demonstrated a significant association with the viral load were smoking and age. Smokers had 6.285 times the probability of having a viral load ≥ 400 copies/ml (P < 0.001). Having an age of less than 45 years carried a 3.313 times the probability of having a viral load ≥ 400 copies/ml (P = 0.024).

Discussion

It is anticipated that for the year 2020, tobacco use will become the top issue in global health[5], highlighting the importance of research in this area. Smoking showed significant associations with one of the parameters: viral load. Patients who were smokers had 6.285 times the probability of having an increase in viral load compared to non-smokers.

In the study by Valiathan et al[17], controlling for viral load it was observed that there existed a characteristically persistent activation of the immune system and an inflammatory response associated with HIV infection that accelerated the *decrease in function of the immune system* and can then increase the risks of further infections. It has been reported that the use of tobacco is associated with a decrease in the immune response, an increase in the inflammatory response, increase in oxidati-

ve stress, opportunistic infections, and possibly, an increase in the replication of HIV-1, a possible decrease in antiretroviral medication effectiveness, and a progressive increase in developing AIDS, concluding that HIV smokers lose more life years to smoking than to the actual HIV infection itself[5,17].

Being that tobacco use is more prevalent in the HIV population[4], this group runs a significant risk. In Table 1, 77.3% of patients with a CD4+ T cell count ≤ 250 cells/mm^3 were smokers. In addition, smokers were 75% of those with a viral load ≥ 400 copies/ml. These results support that the parameters used to measure the effectiveness of the treatment, viral load and CD4+ T cell count, were directly affected by smoking (Table 1 and 2). Taking into account these results, we can affirm that HIV positive patients have a decreased immune system response, leading to an inadequate response to their treatment. We observed that 82.9% of non-current smokers who presented with a viral load < 400 copies/ml were never smokers, which further supports that HIV patients who do not smoke, have a lower amount of the virus in their system (Table 2).

The logistic regression analysis observed in Fig. 1, when compared to the patients 45 years or older, patients younger than 45 years old had a 3.13 times greater probability of having a viral load ≥ 400 copies/ml (P = 0.024). Villante et al[22] reported that younger patients were more prone to be smokers (P < 0.05), also supporting the results found in our study. It is important to consider age as a confounding factor as there was a higher proportion of participants under the age of 45 years old enrolled in the study, and age may have had an effect between the relationship of smoking and viral load.

Table 1. Relationship of CD4+ T cells in smokers, ex-smokers and never smokers.

CD4+ T cells				
Variables	Number	≥ 251 N (%)	≤ 250 N (%)	P-value
Smoker				
Yes	78	61 (40.7)	17 (77.3)	.001
No	94	89 (59.3)	5 (22.7)	
Ex-smoker	16	14 (15.7)	2 (40.2)	.160
Never smoker	78	75 (84.3)	3 (60.0)	

Source: Data collection instrument of the relationship of smoking with the viral load and CD4+ T cell count in HIV patients, 2015.

Table 2. Relationship of viral load in smokers, ex-smokers, and never smokers.

Viral Load				
Variables	Number	< 400 N (%)	≥ 400 N (%)	P-value
Smoker				
Yes	75	48 (38.7)	27 (75.0)	.000
No	85	76 (61.3)	9 (25.0)	
Ex-smoker	15	13 (17.1)	2 (22.2)	.703
Never smoker	70	63 (82.9)	7 (77.8)	

Source: Data collection instrument of the relationship of smoking with the viral load and CD4+ T cell count in HIV patients, 2015.
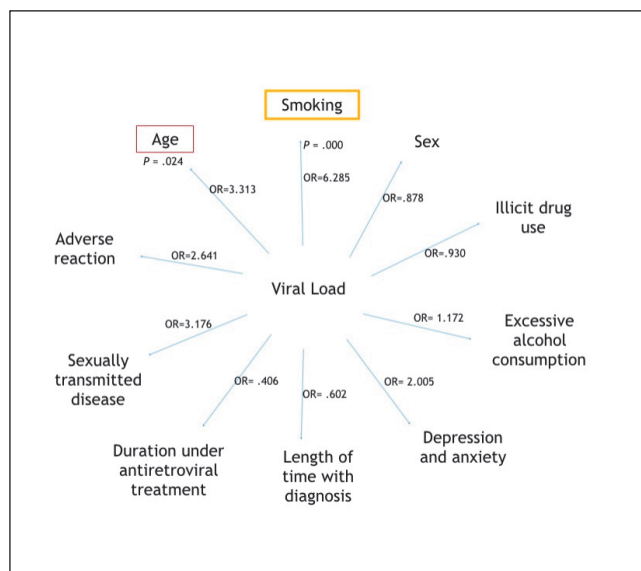
Figure 1. Logistic regression of the viral load and the following variables: smoking, sex, illicit drug use, age, length of time with diagnosis, duration under antiretroviral treatment, adverse reaction, sexually transmitted disease, depression and anxiety, and excessive alcohol consumption.
Source: Data collection instrument of the relationship of smoking with the viral load and CD4+ T cell count in HIV patients, 2015.

The literature reports that in most cases the patients who become infected with HIV are mainly from low income resources and have low education levels[27], therefore lack of awareness could delay their search for medical attention, and as a result, delay their treatment process, leading to an increase in a poor response to the antiretroviral treatment. In agreement with the literature[28], the logistic regression analysis in our study (Fig. 1) showed that there did not exist a significant association between time of diagnosis and the duration under antiretroviral treatment. Likewise, the following variables did not show a significant association with the viral load: sex, depression and anxiety, adverse reaction, a history of sexually transmitted disease, excessive consumption of alcohol, nor illicit drugs use.

In order to incorporate variables valuable to our study, it was of great importance to perform an exhaustive research of the literature[3,6,12,22,29,30,31]. To our knowledge, our study brings new information to Latin American countries, specifically the Dominican Republic. Further strengthening our research, we utilized the two parameters (viral load and CD4+ T cell count) that have been used to determine effectiveness of antiretroviral treatment, however, being that the study was a cross-sectional transverse design, we were not able to determine cause and effect relationships between the variables. In the case of the use of tobacco, we used a questionnaire already validated with which we were able to obtain the necessary information that helped in the design of our study.

Limitations

There were several limitations to our study. The population source was from an institutional system, therefore, there is a risk of potential population bias as the population studied could be healthier than those patients lost to follow up in the program. In addition, future research could explore further analysis regarding demographic or clinical variables from study participants versus the other patients who are also enrolled at the UAI. Furthermore, as the smoker or non-smoker status couldn't be chemically verified, it would be interesting for future studies to assess the nicotine in the patient's blood.

List of abbreviations

AIDS   Acquired Immunodeficiency Syndrome
CDC   Center for Disease and Control
COBE-FACS Comité de Bioética de la Facultad de Ciencias de la Salud
HAART   Highly Active Antiretroviral Therapy
HIV   Human Immunodeficiency Virus
SPSS   Statistical Package for the Social Sciences
UAI   Unidad de Atención Integral
WHO   World Health Organization

Declarations

Ethics approval and consent to participate. The Bioethics Committee, "Comité de Bioética de la Facultad de Ciencias de la Salud (COBE-FACS)", from the Pontifícia Universidad Católica Madre y Maestra approved the study.

Consent for publication. Each participant of the study signed an informed consent prior to beginning the questionnaire in which the purpose of the study was explained. Participants were informed that the results of the study would be used to provide further data on existing research for the benefit of the patient community. The informed consent elaborated by the investigators was reviewed and approved by the Bioethics Committee at the Pontificia Universidad Católica Madre y Maestra. The informed consents signed by the participants were held in the possession of the investigators for confidentiality, and were reviewed and approved by the Bioethics Committee. These informed consents are no longer available, however, the approval and seal of the Bioethics Committee demonstrating that the study met the international and national guidelines, as well as the investigative research guidelines established by the Pontificia Universidad Católica Madre y Maestra is available upon request.

Availability of data and material. The datasets used and analyzed in the study are available upon request from the corresponding author.

Competing interests. The authors declare that they have no competing interests.

Acknowledgments

References

1. Hernández Requejo D, Abad Lamoth Y, Valle Carvajal EB. Linfocitos T CD4+ y carga viral en pacientes VIH/SIDA de la tercera edad que reciben tratamiento antirretroviral. Revista Cubana de Investigaciones Biomédicas. 2013; 32 (2): 139-146.
2. Global HIV & AIDS statistics. UNAIDS. 2018. Available at: http://www.unaids.org/en/resources/fact-sheet
3. Grover KW, Gonzalez A, Zvolensky MJ. HIV symptom distress and smoking outcome expectancies among HIV+ smokers: a pilot test. AIDS Patient Care and STDs. 2013; 27 (1): 17-21.
4. Konfino J, Mejia R, Basombrio A. Estrategias para dejar de fumar provistas por infectólogos a personas con VIH en la ciudad autónoma de Buenos Aires. Revista Argentina Salud Pública. 2012; 3 (12): 23-27.
5. Ande A, Mcarthur C, Kumar A, Kumar S. Tobacco smoking effect on HIV-1 pathogenesis: role of cytochrome P450 isozymes. Expert opinion on drug metabolism y toxicology 2013; 9(11): 1453-1464.
6. Machado-Alba JE, González Santos DM, Vidal Guitart X. Efectividad del tratamiento antirretroviral en pacientes de Pereira y Manizales. Revista de Salud Pública. 2011; 13 (3): 492-503.
7. Global hiv/aids response. Progress report WHO 2011. Available at: http://www.who.int/hiv/pub/progress_report2011/regional_facts/en/index3.html
8. Carribean hiv and aids statistics. AVERT 2015. Available at: http://www.avert.org/caribbean-hiv-aids-statistics.htm
9. Dozier AM, Diaz S, Guido J, Quiñones de Monegro Z, McIntosh S, Fisher SG, Ossip DJ. Cohort study of smoke-free homes in economically disadvantaged communities in the Dominican Republic. Rev Panam Salud Pública. 2014; 35 (1): 30-37.
10. Luu HN, Amirian ES, Scheurer ME. The interaction between smoking status and highly active antiretroviral therapy (HAART) use on the risk of kaposi's sarcoma (KS) in a cohort of HIV-infected men. British Journal of Cancer. 2013; 108: 1173-1177.
11. Friedman MS, Marshal MP, Stall R, Kidder DP, Henny KD, Courtenay-Quirk C et al. Associations between substance use, sexual risk taking and HIV treatment adherence among homeless people living with HIV. AIDS Care. 2009; 21(6); 692-700.
12. Webb MS, Vanable PA, Carey MP, Blair DC. Medication adherence in HIV-infected smokers: the mediating role of depressive symptoms. AIDS Education and Prevention. 2009; 21: 94-105.
13. Health Department: office of infectious diseases. Sexually transmitted disease risks/ HIV/hepatitis questionnaire. New York. 2014. Available at: https://www.health.ny.gov/forms/doh-4336es.pdf. Accessed October 4, 2014.
14. Rico JL, Restrepo M, Molina M. Adaptación y validación de la escala hospitalaria de ansiedad y depresión (HAD) en una muestra de pacientes con cáncer del Instituto Nacional de Cancerología de Colombia. Avances en Medicina. 2005; 3: 73-76.
15. Orozco MJN, Perez Taran B, Barrientos Casarrubias V, Robles Garcia R, Sierra Madero JG. Escala de Ansiedad y Depresión Hospitalaria (hads): validación en pacientes mexicanos con infección por VIH. Psicología Iberoamericana. 2013; 21(2): 29-37.
16. O'Cleirigh C, et al. The Unique Challenges Facing HIV-Positive Patients Who Smoke Cigarettes: HIV Viremia, Art Adherence, Engagement in HIV care, and Concurrent Substance Use. AIDS Behav. 2014; 19(1):178-185.
17. Valiathan R, Miguez MJ, Patel B, Arheart KL, Asthana D. Tobacco smoking increases immune activation and impairs t-cell function in HIV infected patients on antiretrovirals: a cross-sectional pilot study. Plos One. 2014 May; 9 (5): 1-10.
18. Mariano AC, Estrella LM. Como hacer una regresión logística binaria "paso a paso" (II): análisis multivariable. Fabis 2007.
19. Vidrine DJ, Fletcher FE, Buchberg M, Li Y, Arduino RC, Gritz ER. The influence of HIV disease events/stages on smoking attitudes and behaviors: project state study of tobacco attitudes and teachable events. BMC Public Health. 2014; 14: 149.
20. Grover KW, Gonzalez A, Zvolensky MJ. HIV symptom distress and smoking outcome expectancies among HIV+ smokers: a pilot test. AIDS Patient Care and STDs. 2013; 27 (1): 17-21.
21. Encuesta Mundial de Tabaquismo en Adultos. Pontificia Universidad Católica Madre y Maestra: Department of Health Science and Medicine 2014.
22. Villanti A, German D, Sifakis F, Flynn C, Holtgrave D. Smoking, HIV status, and HIV risk behaviors in a respondent-driven sample of injection drug users in Baltimore, Maryland: the besure study. AIDS Education and Prevention. 2012; 24 (2): 132-147.
23. King RM, Vidrine DJ, Danysh HE, Fletcher FE, McCurdy S, Arduino RC, et al. Factors associated with nonadherence to antiretroviral therapy in HIV-positive smokers. AIDS Patient Care and STDs. 2012; 26 (8): 479-485.
24. Harris Ricardo D, Díaz Caballero AJ, Fortich Mesa N. Lesiones bucales en pacientes con VIH/SIDA asociadas a tratamiento antirretroviral y carga viral. Revista Cubana de Investigaciones Biomédicas. 2013; 32 (3): 284-292.
25. Sistema de Vigilancia de Factores de Riesgo del Comportamiento Cuestionario. BRFSS: Centers for Disease Control and Prevention 2013.
26. Alcántara Gutiérrez DI. Factores asociados a la adherencia al TARGA, en pacientes con VIH/SIDA del Hospital Nacional Hipólito Unanue: Lima-Perú 2004-2007. Thesis, Universidad Nacional Mayor de San Marcos. 2008. Available at: http://www.google.com.do/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0CBsQFjAA&url=http%3A%2F%2Fcybertesis.unmsm.edu.pe%2Fbitstream%2Fcybertesis%2F483%2F1%2Falcantara_gd.pdf&ei=C6QwVM6kF8vAggSHvoDAAQ&usg=AFQjCNHqyiMnlGsl4xobRype-TY6-R6gHA
27. Stewart DW, Jones GN, Minor KS. Smoking, depression, and gender in low-income african americans with HIV/AIDS. Taylor & Francis Group. 2011; 37: 77–80.
28. Machado-Alba JE, Vidal X. Effectiveness of antiretroviral treatment in Colombia. Rev Panam Salud Publica. 2012; 32(5): 360-367.
29. Norman LR, Dévieux JG, Rosenberg R, Malow RM. HIV-testing practices and a history of substance use among women living in public housing in Puerto Rico. Journal of the International Association of Physicians in AIDS Care. 2011; 10 (4): 260-265.
30. Davies MA, Boulle A, Technau K, Eley B, Moultrie H, Rabie H, et al. The role of targeted viral load testing in diagnosing virological failure in children on antiretroviral therapy with immunological failure. Tropical Medicine and International Health. 2012; 11(2): 1386-1390.
31. Johnson EN, Roediger MP, Landrum ML, Crum-Cianflone NF, Weintrob AC, Ganesan A. Race/ethnicity and HAART initiation in a military HIV infected cohort. AIDS Research and Therapy. 2014; 11(10).