

# HIV Infection: Plasma Viral Load Intra-treatment in the Era of the “Undetectable = Untransmissible”

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## Abstract

It is widely accepted that HIV-infected subjects are incapable of transmitting sexually the infection while their plasmatic viral load remains undetectable. In order to assess the percentage of HIV-infected patients showing undetectable viral loads during their antiviral treatment we studied a population of patients regularly assisted at a general hospital. A total of 298 patients (162 men; 54.36%) were admitted to the study. The mean age was (mean  $\pm$  standard deviation) 47.83  $\pm$  11.69 years and the mean CD4+ cell count was 693.93  $\pm$  363.87  $\times$  10<sup>6</sup> cells/ml. These variables did not show statistically significant differences between men and women. Plasmatic viral load was undetectable in 230 patients (77.81%). The remaining 68 patients (22.82%) showed a mean of 9856.67  $\pm$  70922 copies/ml. These values were higher in men than in women (17379.39  $\pm$  95521.51 copies/ml vs 895.78  $\pm$  5952.99 copies/ml, respectively;  $p = 0.015$ , Student *t*-test). In line with these findings, CD4+ cell count was significantly lower in men (575.10  $\pm$  345.14 cells/L vs 707.04  $\pm$  373.46 cells/L, respectively;  $p = 0.0019$ , Student *t*-test). 187 out of 231 patients receiving their first antiretroviral treatment showed undetectable viral loads (80,95%), while only 42 out of 67 patients having previously received other antiretroviral schemes had undetectable levels of plasmatic viral load (61,69%;  $p = 0.002$ ,  $\chi^2$ ). These findings show that an important number of patients may keep detectable levels of plasmatic viral load during antiretroviral treatment, being therefore capable of sexually transmitting the infection to their couples.

**Keywords:** HIV; Antiretroviral Therapy; Viral Load; Undetectable-non-transmissible

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**Citation:** Graciela G, Graciela G, Rosana C, et al. (2023) HIV Infection: Plasma Viral Load Intra-treatment in the Era of the “Undetectable = Untransmissible”. *Prensa Med Argent*, Volume 109:2. 394. DOI: <https://doi.org/10.47275/0032-745X-394>

**Received:** March 06, 2022; **Accepted:** March 22, 2023; **Published:** March 27, 2023

## Introduction

Studies conducted in pairs where one of the members is infected by HIV but not the remaining one, show that those infected with HIV are unable to transmit sexual infection while their plasma viral load remains undetectable.

Based on these findings, we study the plasma viral load levels during the TAR in individuals infected with HIV on the opportunity of its periodic consultation for viral load control and CD4+ lymphocyte count, as well as the conditions associated with these results.

## Objectives

Determine viral loading levels in patients under antiretroviral treatment and establish the percentage of patients who continue to have detectable levels of plasma viral load despite antiretroviral treatment. Population under study.

## Materials and Methods

The study included all individuals infected with HIV under-retorted antiretroviral treatment that attended the consultation for periodic viral load control and CD4+ lymphocyte count during the duration of the study. The inclusion was sequential, according to the

consultation order and the patients were not submitted to any other selection criteria.

## Antiretroviral Treatment

The initial antiretroviral treatment consisted of one of the following combinations:

Tenofovir + Lamivudin + Efavirenz or Dolutegravir + Lamivudin, or Dolutegravir + Lamivudin + Tenofovir, or Darunavir + Ritonavir + Emtricitabine + Tenofovir.

The choice of subsequent treatment schemes was based on the results of viral resistance tests and was motivated by therapeutic failure, intolerance, or drug toxicity.

## Laboratory Methods

The plasma viral load was quantified by using COBAS<sup>®</sup> HIV-1 reagents using COBAS 4800 equipment according to the manufacturer's recommendations. This method is based on the amplification and detection by real Time PCR of a fragment of the GAG gene and a fragment of the LTR region of HIV. It has a detection limit of 14.2 copies/ml (23.7 IU/ml) within a dynamic range ranging between 20 copies/ml and 10,000,000 copies/ml (33.3 to 16,700,000 IU/ml).



All laboratory determinations were made from the samples taken on the occasion of the usual medical controls, so this study did not imply any intervention on human beings.

### Statistical Analysis

All values are presented as mean  $\pm$  standard diversion. The statistical significance of the differences between averages was estimated by the Student *t*-test for non-paired data. The statistical significance of the differences between categorical variables was estimated by the  $\chi^2$  test or Fisher's exact significance test when the first one did not be applicable.

### Results

The subjects were admitted sequentially on the occasion of their periodic plasma viral load controls and CD4+ lymphocyte counts in external infectiology offices of an acute general hospital in the city of Buenos Aires.

298 patients, 162 men (54.36%) and 136 women (45.64%) were included. The average age  $\pm$  standard diversion was  $47.83 \pm 11.69$  years, being  $46.61 \pm 12.52$  years in men and  $49.28 \pm 10.48$  years in women ( $p = 0.049$ , Student *t*-test).

The CD4+ lymphocyte count was available in 295 patients with an average value of  $693.93 \pm 363.87 \times 10^6$  cells/L, being  $575.10 \pm 345.14$  cells/L in men and  $707.04 \pm 373.46$  cells/L in women ( $p = 0.0019$ , Student *t* test).

The duration of antiretroviral treatment was known in 297 patients, being an average of  $12.14 \pm 8.09$  years, corresponding to  $11.85 \pm 8.03$  years in men and  $12.49 \pm 8.17$  years in women. These differences did not reach statistical significance ( $p = 0.5$ , Student *t*-test). 66 patients were receiving their first antiretroviral scheme while the rest had received more than one drug combination.

The plasma viral load was undetectable in 230 patients (77.81%). The remaining 68 (22.82%) showed an average of  $9856.67 \pm 70922.11$  copies/ml. When comparing these results by sex, the viral load was undetectable in 119 of the 162 men studied (43.46%) and in 111 of the 136 women (81.62%). These differences did not reach statistical significance ( $p = 0.09$ ,  $\chi^2$  test).

The detectable viral load levels were found in men than in women, being respectively (average  $\pm$  standard diversion) of  $17379.39 \pm 95521.51$  copies/ml in the former, and  $895.78 \pm 5952.99$  copies/ml in the second ( $p = 0.015$ , Student *t* test).

When comparing the average viral load values of individuals who were receiving their first antiretroviral treatment with those who had already received two or more different therapeutic schemes, the results (average  $\pm$  standard diversion) were  $3487.38 \pm 44709.38$  copies/ml vs  $31868.51 \pm 122613.57$  copies/ml. These differences did not reach statistical significance ( $p = 0.07$ , Student *t*-test).

However, when comparing patients who were receiving their first antiretroviral treatment with those who had received more than one antiretroviral treatment scheme, it was found that 187 of 231 individuals who received their first treatment showed undetectable viral loads (80.95%), versus 42 of 67 patients in the group that received further antiretroviral treatments (61.69%;  $p = 0.002$ ,  $\chi^2$  test).

### Discussion

Studies conducted in serodiscordant couples for HIV have analyzed the role that antiretroviral treatment (TARV) and the suppression of

viral load play in reducing the HIV transmission risk.

In this regard, the HPTN 052 study communicated in 2011 that the early start of the TARV reduces the risk of HIV transmission in serodiscordant heterosexual couples compared to those who received late antiretroviral treatment lately. This study contributed the first evidence that a TV Cash could prevent the transmission of HIV, although other authors warned that the HIV sexually transmitted risk persists during the first six months of treatment. Subsequent studies that followed up for 5 years showed that this preventive effect of the TARV is maintained over time while the viral load remains suppressed. These findings were then confirmed by independent studies. In the same vein, a review of the available evidence, made in Switzerland in 2008 found that those infected with the HIV that managed to maintain an undetectable viral load for more than six months do not transmit sexual infection. Taken together, these data indicate that adequate TV plays an important role in the interruption of the sexual transmission of HIV, in addition to the obvious therapeutic benefit for those infected.

In the present study, a significant percentage of infected under TV continued to show detectable levels of plasma viral load despite treatment, therefore retaining the ability to sexually transmit HIV. In our series, the percentage of patients with detectable viral loads was similar in both genres, but these levels were significantly higher in men than in women, thus raising the theoretical possibility that the risk of sexual transmission of HIV was greater when the member infected with the couple belongs to the male gender.

The magnitude of the detectable viral load found in our patients was not related to the number of TRAV schemes previously received, although the possibility of presenting an undetectable viral load was significantly greater in those who received their first TARV. This finding is possibly associated with adherence problems to viral treatment and resistance.

The present study, whose design is not proposed by the analysis of risk factors or adherence and/or resistance to treatment does not allow to extract other conclusions. However, these results highlight that, at least in our environment, a significant percentage of patients with TARV continue More than an antiretroviral treatment.

### Conclusion

These findings reflect the need to maximize therapeutic efficacy during antiretroviral treatment with the objective of achieving and maintaining “undetectable = untransmissible”.

### Conflict of Interest

The authors declare that they have no conflicts of interest. The article was sent with the consent of all authors for their evaluation and publication.

### Ethics Statement

Work has been approved by the ethics committee responsible in the workplace, and does not declare means of financing of the work carried out.

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