

Common Mental Disorders are associated with higher viral load in People Living with HIV

Transtornos Mentais Comuns estão associados a maior carga viral em Pessoas Vivendo com HIV

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ABSTRACT The present study aimed to investigate the association between Common Mental Disorders (CMD) and viral load in People Living with Human Immunodeficiency Virus – HIV (PLHIV) in clinical follow-up. A cross-sectional study was performed with 307 PLHIV aged \geq 18 years who were on antiretroviral therapy at the Specialized Care Service of the city of Santos (SP) in 2016. The dependent variable of the study was the quantification of viral load and the independent variable comprised the minor psychic disorders assessed by the Self-Reporting Questionnaire (SRQ-20). To compare the mean levels of the variables, generalized linear models were performed with significance level of 5%. It is concluded that CMD are associated with a higher viral load among PLHIV in clinical follow-up.

KEYWORDS HIV-1. Viral load. Mental disorders.

RESUMO O presente estudo teve como objetivo investigar a associação entre Transtornos Mentais Comuns (TMC) e carga viral de Pessoas Vivendo com Vírus da Imunodeficiência Humana – HIV (PVHIV) em seguimento clínico. Foi realizado um estudo transversal com 307 PVHIV com \geq 18 anos de idade que estavam em terapia antirretroviral no Serviço de Assistência Especializada do município de Santos (SP) em 2016. A variável dependente de estudo foi a quantificação da carga viral; e a variável independente compreendeu os transtornos mentais comuns, avaliados pelo Self-Reporting Questionnaire (SRQ-20). Para comparação das médias das variáveis, foram realizados modelos lineares generalizados com nível de significância de 5%. Conclui-se que os TMC estão associados a uma maior carga viral entre PVHIV em seguimento clínico.

PALAVRAS-CHAVE HIV-1. Carga viral. Transtornos mentais.

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Introduction

Human Immunodeficiency Virus (HIV) is a retrovirus that infects and progressively destroys immune system cells, especially CD4 T lymphocytes. The reproduction of the virus leads infected cells to death, promoting the destruction of the architecture of lymphoid organs and the immune deficiency characteristic of the syndrome¹.

By 2017, there was, in the world, a total of 36.9 million People Living with HIV (PLHIV). In Brazil, in the same year, there were 866 thousand PLHIV, which represented 2.3% of the worldwide prevalence. During the period, 42 thousand new infections were registered, and it is estimated that 11 thousand deaths related to the virus occurred in the Country, accounting for 42.0% of the diagnoses in Latin America².

In the city of Santos (SP), which between 1980 and 2000 received the title of 'Aids' national capital', at least five new cases of HIV are diagnosed per week³. Although it is currently considered a reference in the fight against HIV with the STI/Aids and Hepatitis Program, the city is still in an epidemic situation. In December 2015, the municipality's Specialized Care Service (SCS) had 5.522 users with HIV alive and registered in the system; of these, 4,717 (85%) were frequent in the assistance³.

With the advent of antiretroviral therapy (HAART), Acquired Immunodeficiency Syndrome (Aids) has gone from an acute disease to a chronic disease. With the control of viral replication, PLHIV have acquired a higher life expectancy and have had fewer opportunistic infections⁴. Currently, Brazil has one of the largest coverage of HAART in the world, with 64.0% of people diagnosed receiving free treatment by the Unified Health System (SUS), regardless of their immunological status².

In most individuals, immune reconstitution is observed shortly after the onset of HAART. In Brazil, in 2017, 85.0% of PLHIV aged 18

years or older who had been on HAART for at least six months had reached viral suppression. In the state of São Paulo, there were 88.0%⁵. However, in spite of the clinical improvement achieved by pharmacological treatment, PLHIV often report great emotional suffering that directly interferes with their health conditions and quality of life⁶.

Among the factors that promote such wear, the chronicity and severity of the disease, the adverse effects of HAART are emphasized, and the need to deal with complex, persistent and uncontrollable stressors⁷, such as discrimination and fear of becoming sick⁸.

According to the World Health Organization (WHO)⁹, Common Mental Disorders (CMD) comprise two main diagnostic categories: depressive disorders and anxious disorders. Symptoms influence the mood and feelings of those affected and differ in relation to their severity and duration.

In the 1970s, WHO conducted a study that aimed to validate low-cost methods for tracking CMD. From this study, the Self-Reporting Questionnaire (SRQ-20) has emerged, an instrument proposed by Harding¹⁰ and recommended for community studies and primary care, especially in developing countries, because they comply with the requirements proposed by the WHO¹¹. For this purpose, the instrument evaluates the presence of 20 psychosomatic symptoms, that is, of physical symptoms (such as pain, tremors and gastrointestinal disorders), whose origin involves emotional mechanisms¹⁰. In the general population, it is estimated that 5.8% of individuals with 18 years of age or older develop depression and that 9.3% have anxiety⁹. Among PLHIV, it is estimated that 50% have at least one episode of depression throughout their lives and that 40% are diagnosed with anxiety disorders¹².

Depression and anxiety represent the most important psychiatric disorders among adults living with HIV. However, such disorders are underdiagnosed because their indicators can be mimicked by physical symptoms of

the infection and HAART. In this regard, the adverse effects of efavirenz, a Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI), act as confounding factors of depression symptoms¹².

It is also known that depressive symptoms are strongly associated with poor adherence to treatment¹³, and may lead to worse control of viral replication. However, there are few studies that evaluate the influence of CMD on the clinical evolution of PLHIV in relation to viral load.

In this context, the present study was carried out with the objective of investigating the association between CMD and viral load of PLHIV in clinical follow-up by the reference service of the city of Santos (SP).

Material and methods

This was a cross-sectional study, in which the population was composed of 2,000 PLHIV linked to and retained in the SCS of the city of Santos (SP), that is, those assisted and clinically monitored by the SCS in the year 2014. In this population, only adult men and women were included in the study, aged 18 years and over, in clinical follow-up by the SCS of Santos (SP) and receiving HAART. Considering a level of significance of 5%, sampling error of 0.05 and admitting variations of $\pm 5\%$, a sample of 292 people was calculated. Estimating a sample loss of 10%, the final sample consisted of 322 people (G^* Power). Fifteen participants who presented incomplete or inconsistent questionnaires were excluded, totaling a sample of 307 people.

Data collection was performed at the SCS itself, from February to June 2016, on alternate days and times (from Monday to Friday, from 8:00 am to 6:00 pm, according to the local assistance schedule). The instrument of data collection consisted of a questionnaire, which was applied in the form of an interview by graduate scholars. The interviews lasted for an average of 45 minutes each, and the

graduates were properly trained to guide the participants, but without interfering in their responses.

Data regarding viral load were obtained through Siscel (Control System for Laboratory Tests of CD4/CD8 and Viral Load), accessed directly at the SCS of Santos. The result of the laboratory examination closest to the date of the interview of each participant was used, and this interval did not exceed six months. This interval was established based on the Clinical Protocol and Therapeutic Guidelines for Treatment of HIV Infected Adults¹², which recommends that the viral load test for laboratory monitoring of PLHIV in clinical follow-up should be performed every six months.

To describe the sample, socio-demographic data were obtained (birth sex, gender identity, age, marital status, education, paid activity and financial difficulties at the end of the month), lifestyle (alcoholism, smoking, use of illicit drugs and practice of physical activity) and HIV infection (time of diagnosis, time of HAART, change of scheme and use of efavirenz).

The study-dependent variable was the viral load quantification using the RT-PCR assay (Abbott Real Time HIV-1). Viral load was considered undetectable when < 50 copies/ml of blood⁵. The independent variable comprised the CMD, evaluated by the validated version and translated into Portuguese of the SRQ-2011. Of the 20 dichotomous questions (yes or no) that make up the questionnaire, those who answered affirmatively to seven or more questions were classified as positive for CMD: 1) Do you have frequent headaches? 2) Do you have lack of appetite? 3) Do you have bad sleep? 4) Do you get scared easily? 5) Do you have shaky hands? 6) Have you been feeling nervous, tense or worried? 7) Do you have poor digestion? 8) Do you have unpleasant sensations in your stomach? 9) Do you have difficulty thinking clearly? 10) Have you been feeling sad lately? 11) Have you been cried more than usual? 12) Do you have difficulty performing your daily activities with satisfaction? 13) Do you have

difficulties reaching decisions? 14) Do you have difficulties at your work (is it painful, causes suffering)? 15) Do you feel unable to play an useful role in life? 16) Have you been lost interest in things? 17) Do you feel like an useless person, without purpose? 18) Have you had the idea to end life? 19) Do you feel tired all the time? 20) Do you feel tired with ease?

The data treatment included the description of the sample studied by the absolute and relative frequencies of the qualitative variables. To test the normality of the quantitative variables, the Shapiro-Wilk test was used. Parametric variables were described by mean and standard deviation (SD), while nonparametric variables were described by median and interquartile range (IQR = P25-P75).

In order to compare viral load averages according to the CMD, generalized linear models (GLM) were carried out, having as adjustment variables: birth sex, age, HIV diagnosis time, HAART time (both in years) and current use

of efavirenz. In all tests, a significance level of p -value <0.05 was adopted. The analyzes were carried out in softwares Stata 12.0 and STATISTICA 7.0.

The study was authorized by the Municipal Health Department of Santos and approved by the Research Ethics Committee of the Catholic University of Santos (n° 1.237.142/2015).

Results

The study included 307 PLHIV aged 21.2-80.2 years and mean of 47.9 years (SD 12.0 years), of which 52.4% were female. Regarding gender identity, 54.9% were identified as women, 49.5% were single, 33.9% had completed secondary school, 60.3% did not exercise paid work and 39.2% mentioned always face financial difficulties at the end of the month (*table 1*).

Table 1. Socio-demographic data of People Living with HIV attended by the Specialized Care Service of Santos (SP). 2016

Sociodemographic data	n (%)
Birth sex	
Female	161 (52.4)
Male	146 (47.6)
Gender identity	
Woman	168 (54.9)
Man	135 (44.1)
Transsexual	1 (0.3)
Transvestite	2 (0.6)
Marital status	
Single	152 (49.5)
Married	83 (27.0)
Divorced	36 (11.7)
Widow/widower	36 (11.7)

Table 1. (cont.)

Education	
Incomplete elementary school	82 (26.7)
Complete elementary school	36 (11.7)
Incomplete secondary school	34 (11.1)
Complete secondary school	104 (33.9)
Incomplete higher education	19 (6.2)
Complete higher education	32 (10.4)
Exert paid activity	
Yes	122 (39.7)
No	185 (60.3)
Financial difficulties at the end of the month	
Never	104 (34.0)
Sometimes	37 (12.1)
Many times	18 (5.9)
Almost always	27 (8.8)
Always	120 (39.2)

Source: Own elaboration.

With regard to lifestyle, 24.4% of the participants were smokers and reported using (10.1%) or have already made used (21.2%) of illicit drugs, with marijuana (19.5%), and

cocaine (17.9%) the most cited drugs; 96.4% refused to consume alcoholic beverages and 81.1% reported not practicing physical activities (*table 2*).

Table 2. Lifestyle of People Living with HIV attended by the Specialized Care Service of Santos (SP). 2016

Lifestyle	n (%)
Alcoholism	
Yes	11 (3.6)
No	296 (96.4)
Smoking	
Yes	75 (24.4)
No	232 (75.6)
Use of illicit drugs	
Yes. I do use	31 (10.1)
I have already used	65 (21.2)
No	211 (68.7)
Which illicit drugs	
Cocaine	55 (17.9)

Table 2. (cont.)

Crack	30 (9.8)
Amphetamine	2 (0.6)
Marijuana	60 (19.5)
Ecstasy	6 (1.9)
Another drug	5 (1.6)
I don't want to talk	2 (0.6)
Practice of physical activity	
Yes	58 (18.9)
No	248 (81.1)

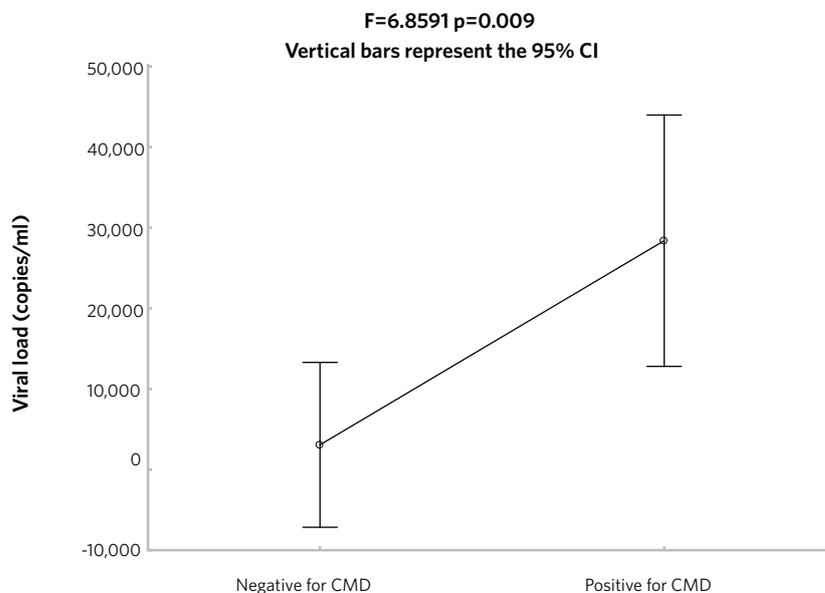
Source: Own elaboration.

Median time to HIV diagnosis was 12.0 years (IQR = 6.0-20.0 years); and the median time of HAART among all respondents was 8.0 years (IQR = 3.0-18.0 years). However, among the 49.7% of the participants who had already changed their therapeutic regimen at least once, the median of the current use of the current regimen was 5.0 years (IQR = 3.0-10.0 years). It was found that 44.2% used a regimen

that included efavirenz.

Of the assessed PLHIV, 28.8% had detectable viral load, and 33.2% were classified as positive for CMD. There was a statistically significant association between CMD and detectable viral load, even after adjustment for birth sex, age, time of diagnosis, time of exposure to HAART, and current use of efavirenz (*figure 1*).

Figure 1. Generalized linear model of the viral load of People Living with HIV attended by the Specialized Care Service of Santos (SP), due to Common Mental Disorders*. 2016



Source: Own elaboration.

* Model adjusted by birth sex, age, time of diagnosis, time of exposure to HAART and current use of efavirenz.

By analyzing the symptoms for CMD tracking investigated by the SRQ-20, six were associated with detectable viral load, such as: poor sleep, unpleasant sensations in the stomach,

difficulty in thinking clearly, feeling sad lately, feeling an useless person and had the idea of ending life (*table 3*).

Table 3. Generalized linear models of the viral load of People Living with HIV attended by the Specialized Care Service in Santos (SP), according to each aspect of the SRQ-20. 2016

Aspects of SRQ-20	F	p
Frequent headaches	0.347	0.556
Lack of appetite	2.137	0.145
Bad sleep	4.763	0.030*
Get easily scared	2.654	0.105
Shaky hands	0.105	0.747
Feel nervous, tense or worried	1.784	0.183
Poor digestion	0.627	0.429
Unpleasant sensations in stomach	6.658	0.010*
Difficulty thinking clearly	5.826	0.016*
Have been feeling sad lately	5.079	0.025*
Have been cried more than usual	3.682	0.056
Difficulty performing daily activities with satisfaction	0.000	0.990
Difficulties reaching decisions	1.854	0.175
Difficulties at work (it is painful, causes suffering)	0.389	0.052
Be unable to play an useful role in life	0.327	0.568
Have lost interest in things	0.081	0.776
Feel like an useless person, without purpose	11.46	0.001*
Have had the idea to end life	23.81	0.000*
Feel tired all the time	0.325	0.569
Feel tired with ease	0.916	0.339

Source: Own elaboration.

* Model adjusted by birth sex, age, time of diagnosis, time of exposure to HAART and current use of efavirenz

Discussion

A statistically significant relationship between CMD and detectable viral load is verified. A similar finding is presented by Leserman and collaborators¹⁴, who verified that depressive symptoms were associated with the rapid clinical progression of Aids in asymptomatic

homosexual men who were not on HAART. Camargo and collaborators¹⁵, on the other hand, identified a negative correlation between viral load and psychic stress, indicating that PLHIV with detectable viral load have fewer mental changes.

In the current situation of controlling the epidemic, which remains a challenge to public health, the evaluation of psychic disorders as

potential confounding factors of the clinical evolution of PLHIV has become essential. As highlighted by the Clinical Protocol and Therapeutic Guidelines for Treatment of HIV Infected Adults¹², recently updated by the Ministry of Health, in addition to the changes resulting from the infection and the adverse effects of HAART mentioned previously, social limitations are among the risk factors for the development of CMD. Among them, are the difficulties related to professional activities and interpersonal relationships, to sexual and loving relationships and to the decision to have children or not¹⁶.

It is also worth noting that, over and above the social limitations related to living with HIV and being on HAART, the clinical history in mental health prior to infection should be considered as an important factor associated with clinical evolution. This aspect, which is difficult to investigate, when added to the aforementioned ones – social issues, adverse drug effects –, can significantly affect adherence to treatment¹².

In addition, it is verified that the relationship between mental health and clinical evolution occurs in a bidirectional way. On the one hand, PLHIV who have psychic disorders become more vulnerable to problems related to the perception and interpretation of the health complications to which they are subject. Thus, it is possible that mental health problems negatively impact clinical evolution even when the individual adheres adequately to HAART. On the other hand, infection, the emergence of comorbidities related to HIV and a worse clinical prognosis may trigger or worsen psychic disorders previously controlled or not yet manifested¹².

Emotional stress can manifest itself both in the form of physical alterations, and sleep disturbances, headaches, fatigue and inappetence, as well as through depressive, anxiety and suicidal ideation¹⁷. In the present study, sleeping poorly and having unpleasant sensations in the stomach were the physical changes significantly associated with higher viral load

among the assessed PLHIV.

During the 1990s, sleep disorders in PLHIV were primarily associated with immunosuppression. However, given its persistence even in situations of optimal control of viral replication, its occurrence has been less attributed to specific infection factors and more related to psychosocial stress¹⁸. Several findings regarding the relationship between immune status and sleep quality in PLHIV are found in the literature. While some studies observe an inverse correlation^{19,20}, others do not find significant results²¹. These differences, as the authors justify, may be due to the absence of a gold standard for the evaluation of sleep of PLHIV.

As with sleep disorders, PLHIV are more prone to the development of gastrointestinal symptoms²². Although its etiology is not fully understood, there seems to be an important relationship between immune status and gastrointestinal disorders. Chronic inflammation, which is caused by HIV itself and can also be induced by prolonged exposure to HAART, promotes the continuous activation of the immune system. As a consequence, there is a homeostatic imbalance of the lymphoid tissue associated to the intestine²³.

With regard to tracking symptoms for depressive and anxious disorders, scores on difficulty in thinking clearly, feeling sad lately, feeling unhelpful, and having the idea of ending life were significant. These symptoms may be associated with uncertainties in disease progression, fear of physical changes, pain, suffering, and death. When prolonged, they constitute a pathological picture that generates professional and/or social damages¹².

Suicidal ideation, in turn, arises in many cases of depressive symptomatology. In studies investigating suicidal ideation among PLHIV, it was found that the death wish is strongly correlated with depression scores¹⁵. For this reason, it can help to distinguish the symptoms of infection and the adverse effects of HAART from a psychopathology¹².

Compared with WHO estimates⁹ for the

general population, the present study found a high prevalence of CMD among participants. Reis and collaborators²⁴, when assessing PLHIV in São Paulo (SP), found a prevalence of 42.3% of depressive and anxious symptoms. The authors also found an association between symptoms and CD4 T lymphocytes <200 cells/mm³, but did not assess the viral load of the participants.

About 30% of participants had detectable viral load, a percentage similar to that reported in the HIV5 Clinical Monitoring Report for PLHIV aged 18 years or older on HAART for at least six months. However, data referring to the year 2015, reported by the SCS of Santos, indicate that 55% of PLHIV using HAART were virally suppressed³. Based on these results, it is possible to observe that the percentage of PLHIV in viral suppression in the municipality was well below the state of São Paulo and the Country in the year 2016, when the data were collected, 85% and 84% respectively. However, the observed reduction in the percentage of detectable viral load in the municipality, from 55.0% in 2015 to 28.8% in 2016, can be attributed to the frequent campaigns of prevention and testing for diagnosis and early treatment of HIV promoted by the National Coordination Centre for Communicable Disease Control.

The occurrence of psychiatric disorders and worst indicators of the clinical evolution of PLHIV also seems to be associated with the use of psychoactive substances, smoking, sedentary lifestyle and unbalanced eating¹². In this aspect, the high prevalence of sedentarism, smoking and drug use verified by the present study also deserve attention.

The prevalence of sedentary PLHIV in this study far exceeds that observed in the general population. According to the National Health Survey – PNS 2013²⁵, 46.0% of adults are considered insufficiently active. In a systematic review of the effects of different types of exercises on PLHIV, Gomes-Neto and collaborators²⁶ found that regular practice contributes positively to physical, personal and social aspects, minimizing stress, improving

the perception of one's own abilities and satisfaction with life. Ferreira and Ceolim²¹ also highlight sleep regulation, preservation of immune function and reduction of the adverse effects of HAART.

Regarding smoking, according to data from PNS 2013²⁵, 15.0% of Brazilian adults use products derived from tobacco daily or occasionally. Thus, like the present study, many authors report prevalence up to two times bigger among PLHIV compared to the general population^{22,27,28}.

Finally, in relation to illicit drugs, the prevalence of PLHIV that they used or have already used was about four times superior than that observed in the general population. According to the World Drug Report 2017²⁹, 5.0% of the adult population have already used drugs at least once in their lifetime. Data from the II National Survey on Alcohol and Drugs (Lenad)³⁰ indicate that 5.8% of Brazilians have ever used drugs and that 2.5% used them in the last 12 months that preceded the study. As in the above surveys, marijuana represented the main substance used.

The results presented reinforce the importance of mental health care for PLHIV as part of a set of non-pharmacological interventions aimed at optimizing the response to HAART and stimulating the active search for a healthier lifestyle.

Although the present study is of extreme relevance to public health, it presents some limitations that need to be punctuated. The instrument used to track CMD evaluates the current presence of psychosomatic symptoms, while the viral load quantification test used in the present study may have been performed within an interval of up to six months. Although this is the range recommended by the current guidelines for clinical HIV monitoring, this difference between the time of the test and the implementation of the questionnaire may represent a possible confounding factor for the reported association. Another limitation is the impossibility of establishing a temporal relation of cause and effect between

the evaluated variables. On the other hand, the results found are supported by previous studies^{8,12-14,16,17}, strengthening this way the associations found. Furthermore, due to the scarcity of data on the topic addressed here and the current situation of the HIV epidemic, studies of this nature are fundamental to raise hypotheses and provide subsidies for other types of study³¹. In this aspect, a strong point of this study is the description of a significant sample of PLHIV using HAART in relation to the CMD tracking and clinical evolution, as well as in the identification of a significant association between these stated variables. From the results presented, it will certainly be possible to contribute to the discussions of public policies to promote the mental health of this population.

Conclusions

CMD are associated with a higher viral load among PLHIV in clinical follow-up. Given the above, the need for investigation protocols and management of mental disorders to better understand their effects on the clinical evolution of PLHIV is emphasized. Early diagnosis and appropriate treatment may significantly contribute to a better outcome of co-morbidities associated or not with HIV.

Collaborators

Nogueira LFR (0000-0002-0230-3684)* contributed to the design, planning, analysis

and interpretation of data; critical review of content; and approval of the final version of the manuscript. Pellegrino P (0000-0003-3194-4082)* contributed to the critical review of the content and approval of the final version of the manuscript. Duarte AS (0000-0002-0126-8557)* contributed to the critical review of the content and approval of the final version of the manuscript. Inoue SRV (0000-0001-7823-1923)* contributed to the critical review of content and approval of the final version of the manuscript. Marqueze EC (0000-0002-4987-7757)* contributed to the design, planning, analysis and interpretation of data; critical review of content; and approval of the final version of the manuscript. *Orcid (Open Researcher and Contributor ID).

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