

Original Research Article

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Comorbidities and Functional Impairment among People Living With HIV in Belém, Pará, Amazon Region of Brazil

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ABSTRACT

Keywords

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This study has investigated the relationship between clinical parameters and functional status for activities of daily living (ADL) in 364 people living with HIV/AIDS (PLWHA) in Belém, northern Brazil. In total, 238 men (65.4%) and 126 women (34.6%) were enrolled in this survey. Most participants (87.4%) were considered with functional independence, 11.8% were semi-dependent and 0.8% were fully dependent. Tuberculosis, neurotoxoplasmosis and syphilis were the most common HIV-associated comorbidities and cumulative comorbidities were linked to lower independence. Low CD4⁺ count and long duration of HIV infection were both related to decreased independence. Women were more affected by low mood/demotivation than men, the last had higher employment rates and more access to higher education, which may have contributed to a better emotional status. We concluded that duration of HIV infection, low CD4⁺ count and history of HIV-associated comorbidities affects functional status and compromise the independence of PLWHA.

Introduction

It is estimated that around 36.9 million people worldwide are infected with the human immunodeficiency virus 1 (HIV-1), and regardless the advances in treatment and preventive politics, this number is still rising [Cobbing *et al.*, 2015; Huang *et al.*, 2015].

The introduction of highly active antiretroviral therapy (HAART) was a watershed in the history of HIV infection and acquired immune deficiency syndrome (AIDS), which significantly increased the survival of people living with HIV/AIDS (PLWHA). Despite it, opportunistic infections and other HIV-associated comorbidities are still very

common in HIV/AIDS patients, and they are considered a serious problem of public health worldwide [Carvour *et al.*, 2015; Heaton *et al.*, 2010; Mayo *et al.*, 2016; Tan *et al.*, 2012].

PLWHA may experience the loss of functional capacity and physical independence; cognitive decline; anxiety; depression; and impairment in social interaction, self-stem and communication [Mayo *et al.*, 2016; DubÈ *et al.*, 2005].

The concept of functional capacity can be defined as the capability of performing tasks and activities that are necessary or desirable in people's life and required for performing activities of daily living (ADL) in an independent way. ADL include basic routine tasks, such as eating, dressing, walking and performing personal hygiene. [Carioli and Teixeira, 2014; Erlandson *et al.*, 2014].

One way to assess the quality of life (QoL) of people is using evaluation instruments, such as the Functional Independence Measure (FIM). FIM is a well-known assessment tool used to evaluate patients' physical, psychological and social function. The FIM can generate a profile based on the degree of independence of subjects to accomplish several tasks like self-care, locomotion, sphincter control, communication and social interaction. This tool has been used in studies in Brazil [Machado *et al.*, 2013; Riberto *et al.*, 2004] and other countries in the world to assess patients' disability [Aydin *et al.*, 2016; Vanbellingen *et al.*, 2016].

This study aimed to investigate the degree of functional independence to perform ADL in PLWHA who were assisted in a specialized reference center in Belém, northern Brazil, and to correlate the clinical and epidemiological characteristics of PLWHA with HIV-associated comorbidities and clinical parameters.

Materials and Methods

Study Design and Sampling

It was a cross-sectional study in PLWHA who were being assisted in the Centro de Atendimentoem Doenças Infecciosas Adquiridas (CASA-DIA) in Belém, Pará, Amazonregion of northern Brazil, between June-October 2016. The inclusion criteria were: age between 18 and 54 (working age), confirmed HIV infection, voluntary participation of subjects and signature of the patient informed consent form. The exclusion criteria included patients with severe neurological and cognitive impairment who were unable to answer the questionnaire in an appropriate way.

Sample Size and Ethical Aspects

Sample size calculation was based on the estimative of individuals enrolled in CASA-DIA in 2015 (approximately 7,108 patients). The sampling error (ϵ) assumed in this calculation was 5% and the statistical power adopted was 80%, which resulted in a minimum sample size of 364 participants. The objectives of this study were explained to all patients, and those who agreed to participate; signed the patient consent form and answered a structured epidemiological questionnaire (through a guided interview) applied by an occupational therapist. The questionnaire included demographic (age, sex, educational background) and epidemiological information (time of diagnosis of HIV-1 infection, treatment with HAART and aspects of social life). Medical history regarding HIV-associated comorbidities, CD4⁺ T cells (CD4⁺) counts and plasma HIV-1 viral load was obtained from the medical records. The study was approved by the ethics committee from the Instituto de Ciências da Saúde, Universidade Federal do Pará, under number CAAE 56117616.0.0000.0018.

Functional Assessment and Medical History

The functional status of participants was evaluated by means of FIM, which was used to assess the overall performance in ADL, motor and cognitive parameters. The FIM is a validated tool that quantitatively assesses individuals' degree of independence in several areas such as self-care, sphincter control, locomotion, communication and social interaction [Riberto *et al.*, 2004]. All participants were interviewed using a standard questionnaire commonly used to assess ADL and each of the evaluated activities received a score ranging from 1 (total dependence) to 7 (total independence). Data from HIV-associated comorbidities and clinical parameters from blood tests were retrieved from the medical records.

Statistical Analysis

The clinical-epidemiological and laboratory data were entered into a database using Microsoft Access 2013 software. Frequency tables, percentages, means and standard deviations were used to present the results. The degree of individual independence in relation to duration of HIV infection, history of comorbidities, CD4⁺ count, and HIV viral load using the Chi-Square test at a significance level of 5%.

Results and Discussion

A total of 386 subjects were initially enrolled and after consideration of inclusion/exclusion criteria, 364 individuals were included in this survey. From those participants, 238 (65,4%) were male and 126 (34,6%) were female. The mean age was 31.4 for men, with the age range of 27-35 being the most prevalent with 42.4%. The average age for females was 7.1 years higher than men(38.5), while the most prevalent age range for women was 36 to 44 (47%).

Regarding to marital status, the majority of the participants were single, males (94.1%) and females (77.8%). The educational background indicated most men (56.7%) and women (57.9%) had completed the high school (10 years of formal education or more). Furthermore, 23.9% of men reported having some level (complete or incomplete) of higher education (13 years of formal education or more). Illiteracy was reported among women only (1.6%). The monthly familial income was up to 1 minimum Brazilian wage (equivalent to 252 USD at the time of the study was carried out) for 84.1% of women and 60.1% of men, which should take in consideration that the unemployment rate was higher among women (57.9%) than in men (45.0%).Socio-demographic, HAART treatment, viral load and CD4⁺count data are described in Table 1.

In relation to the timing of diagnosis of HIV-1 infection, most men (69.7%) and women (63.4%) were in the interval between 1-5 years of confirmed HIV infection, while 10.9% of men and 11.9% of women have had known HIV infection for more than 10 years. Although HAART was abandoned at least once in 21% of men and 34.2% of women, most of the individuals were using HAART during the time of the survey, and only 2.1% of men and 4.8% of women had not begun the antiretroviral therapy. The CD4⁺ counts ranged from 101 to 500 cells/mm³ in 49.2% in either males and females. The plasma HIV-1 viral load was determined as a log₁₀ and ranged from <1.69 log₁₀ to 4.00 log₁₀. A CD4⁺ count below than 4.00 log₁₀ was considered undetectable. The most prevalent group for men and women had undetectable viral load and women had around 40% more participants with HIV viral load above 10,000 than men, proportionally (Table 1).

A total of 242 participants (66.5%) have had at least one HIV-associated comorbidity before this survey, 165 (68.2%) were male and

77 (31.8%) were female, with a slightly higher ratio of comorbidities in men than in women (2.2:1), taking in consideration a higher proportion of men versus women (1.9:1) in this study. The most common HIV-associated comorbidity in male was syphilis (44/165; 26.7%), while tuberculosis (22/77; 28.6%) was the most common among women. In male, syphilis, tuberculosis and neurotoxoplasmosis were the most prevalent comorbidities, while in women, the top 3 were the same, but in a different order: tuberculosis, neurotoxoplasmosis and syphilis. Other comorbidities have also been reported at a lower frequency. They were grouped and named as others, which included: rheumatoid arthritis, leprosy, meningitis, epilepsy, mental disorder and malaria (Table 2).

Social life is an important criterion that influence the life of PLWHA, because it not only affects the overall QoL after HIV diagnosis but can also interfere in the adherence to HAART. Most men and women reported to be engaged in social activities, such as going out, social events, family meetings, and friends or community activities. They also reported having support of their friends and family to taking part in these activities and other aspects of life in a similar high proportion of around 83%. However, despite having similar rates of social life and family/friends support, women were more emotionally affected by HIV infection and experienced significant higher distribution of low mood/demotivation than men ($p < 0.0067$) (Table 3).

Results from functional independence measures (Table 4) showed that the majority of participants demonstrated to be satisfactory independent to perform ADL, such as personal care (food, hygiene, dressing), locomotion, transportation, communication and cognition. Twenty-four men (10.1%) and 19 women (15.1%) were classified as semi-dependent

(moderate dependence), with only two men (0.8%) and one woman (0.8%) being considered as fully dependent, which means they need maximum or total help to carry out their daily activities.

To correlate the functional status (degree of independence) with the presence of comorbidities, duration of HIV infection diagnosis, CD4⁺ count and plasma viral load, the participants were divided in two groups: independent and dependent (semi-dependent and fully dependent).

Results showed that the history of HIV-associated comorbidities, duration of HIV infection and low CD4⁺ count (<100) were associated with some loss of independence, only the HIV viral load did not significantly affect the level of independence. The participants who never had a history of comorbidities were independent in 95.6% of the cases, while they experience a growing number of comorbidities, the independence level drops significantly (Table 5). The duration of HIV infection also affected the independence of the participants. During the first year after diagnosis, PLWHA reported to be very independent (94.1%), but according the time passes, the dependence rate grows to 2.8 times between 1-5 years, 2.3 times between 5-10 years, and 3.8 times after 10 years (Table 5).

Low CD4⁺ count (<100) was associated with a higher dependence rate. Individuals who had the CD4⁺ count (<100) reported to be dependent in 33.3% of the cases, while when the CD4⁺ count was >100, the highest dependence rate was 16.7%, surprisingly found in patients with CD4⁺ count >10,000 (Table 5).

There is limited information regarding the impact of HIV infection and HIV-associated comorbidities in PLWHA in Brazil.

Table.1 Socio-demographic and clinical data in PLWHA in Belém, northern Brazil

Variables	Male		Female	
	n	(%)	n	(%)
Age				
18 – 26	44	18.5	22	17.4
27 – 35	101	42.4	38	30.2
36 – 44	59	24.8	47	37.3
45 – 54	34	14.3	19	15.1
Educational background				
Illiteracy	0	0	2	1.6
Elementary and/or middle school	46	19.4	40	31.7
High school	135	56.7	73	58
Higher education	57	23.9	11	8.7
Marital status				
Single	224	94.1	98	77.9
Married	13	5.5	20	15.9
Widowed	1	0.4	4	3.1
Divorced	0	0	4	3.1
Employed				
Yes	131	55	53	42.1
No	107	45	73	57.9
Monthly family income^a				
Upto 1 minimum wage	143	60.1	106	84.1
1-3 minimum wages	82	34.5	19	15.1
>3 minimum wages	13	5.4	1	0.8
Duration of HIV infection				
<1 year	53	22.3	25	19.8
1-5 years	113	47.5	55	43.7
5-10 years	46	19.3	31	24.6
>10 years	26	10.9	15	11.9
HAART treatment				
Yes	233	97.9	120	95.2
No	5	2.1	6	4.8
Duration of HAART				
<1 year	68	29.2	30	25
1-5 years	108	46.3	58	48.3
5-10 years	34	14.6	23	19.2
>10 years	23	9.9	9	7.5
Interruption of HAART				
Yes	49	21	41	34.2
No	184	79	79	65.8
CD4⁺ count^b				
<100	10	4.2	11	8.7
101-500	117	49.2	62	49.2
501-1,000	91	38.2	43	34.1
>1,000	20	8.4	10	8
HIV viral load^b				
Undetectable (<40)	101	42.4	45	35.7
40-500	63	26.5	30	23.8
501-10,000	34	14.3	21	16.7
>10,000	40	16.8	30	23.8
Total	238	100	126	100

^aMonthly family income in multiples of minimum Brazilian wage (equivalent to 252 USD) at time of data collection. ^bResults are referred to the last test count before data collection

Abbreviations: PLWHA, people living with HIV/AIDS; HAART, highly active antiretroviral therapy.

Table.2 HIV-associated comorbidities in PLWHA in Belém, northern Brazil

HIV-associated comorbidity	Male		Female	
	n	(%)	n	(%)
Syphilis	44	26.7	13	16.9
Tuberculosis	38	23	22	28.6
Neurotoxoplasmosis	36	21.8	16	20.8
Viral hepatitis	24	14.6	5	6.5
Diabetes	4	2.4	5	6.5
Stroke	3	1.8	6	7.8
Hypertension	1	0.6	2	2.6
Others	15	9.1	8	10.3
Total	165	100	77	100

Table.3 Psychosocial characteristics and functional independence measures in PLWHA in Belém, northern Brazil

	Male		Female		p ^a
	n	(%)	n	(%)	
Participation in social activities					
Yes	168	70.6	92	73	0.7145
No	70	29.4	34	27	
Family/friends support					
Yes	199	83.6	105	83.3	0.9363
No	39	16.4	21	16.7	
Low mood/demotivation					
Yes	57	24	48	38.1	0.0067
No	181	76	78	61.9	
Total	238	100	126	100	

^aChi-squared test

Table.4 Functional independence measures of PLWHA in Belém, northern Brazil

Independence level	Male		Female	
	n	(%)	n	(%)
Independent	212	89.1	106	84.1
Semi-dependent (moderate dependence)	24	10.1	19	15.1
Dependent (fully dependent)	2	0.8	1	0.8
Total	238	100	126	100

Table.5 Comparison between functional independence status and clinical parameters in PLWHA in Belém, northern Brazil

	Independent		Dependent ^a		p ^b
	n	(%)	n	(%)	
HIV-associated comorbidities					
none	172	95.6	8	4.4	<0.0001
1	117	86.0	19	14.0	
2	24	66.7	12	33.3	
>2	5	41.7	7	58.3	
Duration of HIV infection					
<1 year	128	94.1	8	5.9	0.0167
1-5 years	109	83.2	22	16.8	
5-10 years	56	86.2	9	13.8	
>10 years	25	78.1	7	21.9	
CD4⁺ count^c					
<100	14	66.7	7	33.3	0.0076
101-500	155	86.6	24	13.4	
501-1,000	124	92.5	10	7.5	
>1,000	25	83.3	5	16.7	
HIV viral load^c					
Undetectable (<40)	163	87.2	24	12.8	0.748
40-500	47	90.4	5	9.6	
501-10,000	46	83.6	9	16.4	
>10,000	62	88.6	8	11.4	

^aDependent group include dependent and semi-dependent patients

^bChi-squared test

^cResults are referred to the last test count before data collection

The present study is pioneer in evaluating this information in northern Brazil and also to investigate the functional capacity for ADL in PLWHA according to an already well-established protocol [Pretz *et al.*, 2016]. Furthermore, we analyzed the consequences of HIV-associated disability and its effects in patients' quality of live.

Our results showed a low prevalence of individuals with functional dependence. Most individuals considered themselves as independent (87.4%), which seems to be high compared to other studies that reported an independence level varying from 9.76 to 14.51 on a scale range from 4 to 20 [Bayisa

and Wubshet, 2016; Passos and Souza, 2015; Hipolito *et al.*, 2017]. These authors used the World Health Organization Quality of Life Instrument, brief version (WHOQOL-HIV Bref) [Bayisa and Wubshet, 2016; Passos and Souza, 2015; Hipolito *et al.*, 2017]. In our study, 11.8% were considered semi-dependent and only 0.8% fully dependent. Educational background seems to play a role in physical and psychological ways that shape the way that PLWHA face the disease, which in turn affects the level of independence and the QoL. In this study 23.9% of male and 8.7% of female had access to higher education, and not surprisingly, women suffered more than men from low

mood/demotivation. The elevated level of independence observed in our study may be due to the high prevalence of participants who attended a higher education course (overall 18.7%), which is between around 1.5 to 2 times higher than what was found in other studies with 9.8% [Passos and Souza, 2015] and 12.1 [Bayisa and Wubshet, 2016]. Some studies have reported that PLWHA have difficulty to get or maintain their employment; they experience elevated levels of stress, which reflects negatively in the quality of lives of these individuals [Benedict *et al.*, 2000; Blackstone *et al.*, 2012; Ferreira *et al.*, 2012; Kamat *et al.*, 2013].

Interestingly, this study found that mostly of PLWHA are engaged in social activities and had the support of friends and/or family members to do so. Keeping an active social life and a good social interaction with family and friends are key factors to deal with all the challenges associated with the disease itself and for keeping the adherence to the antiretroviral treatment. On the other hand, lack of this support is associated with a higher likelihood to abandon the treatment or leading to social exclusion, thereby acceleration the patients' functional decline [Ferreira *et al.*, 2012; Kamat *et al.*, 2013]. In this study, most subjects reported never having abandoned the HAART, which may reflect in a better QoL.

Despite the advances in HIV therapy, HIV-associated comorbidities are still common in PLWHA and these are the main causes of sequelae and disabilities experienced by these individuals [Zingmond *et al.*, 2017]. Most of participants in this study, regardless of gender, have experienced some sort of HIV-associated comorbidity, which was linked to functional decline. However, only 12.6% of the participants were classified as dependent or semi-dependent that required some type of assistance. Functional dependence was linked with HIV-associated comorbidities, such as

syphilis, tuberculosis and neurotoxoplasmosis; duration of HIV infection; and low CD4⁺ count [Blackstone *et al.*, 2012; Ferreira *et al.*, 2012; Kamat *et al.*, 2013; Troncoso and Conterno, 2015; Cho *et al.*, 2015].

The main functional disabilities were related to tasks that required physical efforts such as walking, climbing stairs, locomoting and commuting according to the FIM. Even in cases when a patient has achieved the maximum score in the FIM (considered independent), this does not mean that the patient does not have a clinical complaint [Erlandson *et al.*, 2014; Benedict *et al.*, 2000; Blackstone *et al.*, 2012]. However, even facing some difficulties, this patient could perform all the ADL without external aid. The physical impairment in ADL, which are simpler and more meaningful, is related to an overall weaker state.

Preventive measures seem to be important to avoid neurological disabilities and keep PLWHA with a better QoL and longer productive life. Although the techniques used to prevent neurological disability do not alter the natural course of HIV infection, they often increase the functional performance of these individuals. Identifying the problems and disabilities presented by PLWHA is essential for a proper referral to special care, which includes preventive measures, basic external support and rehabilitation services. Early detection of physical and/or functional disabilities is important to ensure a better QoL for these individuals.

Identification of socio-demographic characteristics, functional and independence status of PLWHA are valuable information to establish specific public health policies and they are an efficient way to provide aid to these patients and improve their QoL [Machado *et al.*, 2013]. An early

identification of any functional disability is fundamental to initiate therapeutic intervention that can minimize further complications and prevent possible sequelae.

In summary, we observed that the independence status of PLWHA on their ADL are related to the presence of HIV-associated comorbidities, duration of HIV infection and CD4⁺ count.

We observed that the presence HIV-associated comorbidities (combination of 2 or more are even more debilitating) increase the level of individuals' dependence due to motor and neurological disabilities.

Positive and interesting facts found in our study are that most of the participants reported to have an active social life and received family/friends support, they also demonstrated more access to a higher education, which combined may reflect in a better way to face the disease, improve the QoL, and increase the adherence to the antiretroviral therapy.

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Conflicts of interest

There are no conflicts of interest.

Ethical approval

The study was approved by the ethics committee from the Instituto de Ciências da Saúde, Universidade Federal do Pará, under number CAAE 56117616.0.0000.0018.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

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