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EXTENDED ABSTRACT

A12 Are demographic, clinical and psychosocial factors and depression symptoms associated with dementia risk among patients with HIV in Portugal?

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Introduction:

The global situation regarding Human Immunodeficiency Virus (HIV) infection has changed substantially, making Acquired Immunodeficiency Syndrome (AIDS) a chronic disease, with consequences at the physical, psychological (adjustment difficulties, psychological distress) and social (withdrawal, stigma, lack of social support) levels [1].

At the brain level, HIV infection can cause several problems, affecting up to half of people with this infection - known as HIV-associated neurocognitive deficits (HAND) [2]. HIV-associated dementia (HAD) is more prevalent in people living with HIV who have severe immunosuppression, high viral loads in the cerebrospinal fluid and advanced HIV, as indicated by anaemia and hypoalbuminemia [3]. Research evidence worldwide has consistently reported a high prevalence of HAD among people living with HIV. The International HIV Dementia Scale (IHDS) is among the most commonly and internationally used screening scales for HAD due to its acceptable properties observed in terms of good reliability and validity, and also due to its simplicity, and limited requirement of language proficiency and training [4].

In this work, a retrospective study is performed in Portugal to identify possible clinical, psychological, social and demographic characteristics as well as symptoms of depression that significantly affect the risk of dementia in patients with HIV.

Methods:

A non-probabilistic sample of HIV patients was selected to this study, following criteria: age over 18 years old, undergoing antiretroviral treatment, who agreed to participate in this study, with the permission of the respective doctor. People with cognitive disorders that prevented them from understanding the objectives of the study, as well as giving free and informed consent, were excluded.

The data were acquired (March 2017 to July 2020) by e-interviews, conducted by specialists in mental health, based on the data collection protocol that included the following tools (1) questionnaire for the collection of sociodemographic and health data/risk behaviours; (2) the Simplified Medication Adherence Questionnaire (SMAQ); (3) the International HIV Dementia Scale; (4) Social Support Scale for People with HIV/AIDS; (5) Brief Inventory of Symptoms (BSI) and (6) Barthel Index.

At the beginning of the data analysis, descriptive univariate statistical measures were calculated for different characteristics. Continuous data, such as time since HIV diagnosis, emotional support, instrumental support, global severity index and nine subscales of symptoms of depression were summarized using median and interquartile range (IQR). For categorical variables, percentages and counts were used.

Then, bivariate statistical analyses were conducted. Namely, the association between HAD and demographic (age, sex, marital, work, education and the living with status), clinical (time since HIV diagnosis, HIV hospitalization, time antiretroviral therapy ART initiation, adherence to therapeutic regime, hepatitis B infection, hepatitis C infection, presence of other diseases, history of opportunistic diseases and people support) and psychosocial (emotional support, instrumental support and global severity index) characteristics were assessed using the t-test for normally distributed continuous variables, the Mann-Whitney-U test for non-normally continuous variables and the chi-square test for categorical variables. Subsequently, association between HAD and nine symptom dimensions of depression (somatization, obsession-compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism) were additionally analysed using the Mann-Whitney-U test.

At the end, logistic regressions were applied for searching relevant factors which were influencing high risk of HAD (dependent variable). Odds ratios (OR) and 95% confidence intervals (CI) were calculated for cross tabulation.

Keywords:
HIV, AIDS, Dementia, IHDS, Portugal.

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Whenever the p-value P <0.05, the results were considered statistically significant. Data were analysed using R version 4.0.4.

Results:

A total of 255 patients with HIV infection of which 149 (58%) of patients with HIV had probable high risk HAD, based on the cut-off of <10.5 on the IHDS, integrated in this study. Nearly 81% of participants were male with ages ranged from 21 to 86 years, with a mean of 47 years (SD=10.07).

HAD was not associated with none of the six demographic variables (P>0.05) (Table 1).

Table 1 - Sociodemographic characteristics and risk of HIV-associated dementia (HAD).

Sociodemographic characteristics	Risk of dementia		*p* value	OR (95% CI)
	Low risk (n = 106)	High risk (n = 149)		
	Mean ± SD	Mean ± SD		
Age	49 ±10.05	47 ± 10.07	0.13	0.98 (0.95-1.00)
Sex	n (%)	n (%)		
Female	25 (23.6)	23 (15.4)	0.13	1
Male	81(76.4)	126 (84.6)		1.69 (0.90-3.19)
Marital status	n (%)	n (%)		
Single	44 (41.5)	63 (42.3)	0.23	1
Married/live as a couple	39 (36.8)	42 (28.2)		0.75 (0.42-1.34)
Divorced/separated/widowed	23 (21.7)	44 (29.5)		1.33 (0.71-2.54)
Work status	n (%)	n (%)		
Employed	48 (45.3)	72 (48.3)	0.42	1
Unemployed	34 (32)	46 (30.9)		0.90 (0.51-1.60)
Retired	19 (18)	29 (19.5)		1.02 (0.51-2.03)
Other	5 (4.7)	2 (1.3)		0.27 (0.04-1.29)
Education status	n (%)	n (%)		
Up to 4 years	48 (45.3)	71 (47.6)	0.72	1
Up to 9 years	35 (33)	46 (31)		0.89 (0.50-1.58)
Up to 12 years	20 (18.8)	23 (15.4)		0.78 (0.38-1.58)
High school	2 (1.9)	7 (4.7)		2.37 (0.54-16.34)
Other	1	2 (1.3)		1.35 (0.13-29.58)
Living with	n (%)	n (%)		
Alone	32 (30.2)	48 (32.2)	0.83	1
Family	74 (69.8)	101 (67.8)		0.90 (0.53-1.55)

Abbreviations: ART, antiretroviral therapy; CI, confidence interval; IQR, interquartile range; SD, standard deviation.

HIV-associated dementia was associated with the adherence level to therapeutic regime (OR=1.95, 95% CI: 1.18-3.25, P=0.01), where patients with good adherence were less likely to have probable high risk HAD than those with moderate adherence. However, the remaining clinical variables were not associated with probable HAD (Table 2).

There was a statistically significant association between HAD and emotional support (OR=0.78, 95% CI: 0.60-0.99, P=0.04) and global severity index (OR=1.64, 95% CI: 1.12-2.43, P=0.007) (Table 2). Therefore, patients who received strong emotional support were less likely to have probable high risk HAD than those who received poor emotional support, but those presenting larger global severity index were more likely to have probable high risk HAD.

In the analysis of the nine symptom dimensions of depression, there were a statistically significant association between HAD and obsessive compulsive (OR=1.75, 95% CI: 1.22-2.55, P=0.003), interpersonal sensitivity (OR=1.49, 95% CI: 1.11-2.05, P=0.02), paranoid ideations (OR=1.40, 95% CI: 1.02-1.93, P=0.02), psychoticism (OR=1.45, 95% CI: 1.45-2.02, P=0.04) (Table 3).

Discussion:

Patients with dementia have complicated issues and symptoms in many domains that interfere with daily activities [Livingston, et al, 2020)]. In these cases, patients should be considered as a whole, as well as their family caregivers, and interventions should be individualized. Evidence is accumulating for the effectiveness, at least in the short term, of psychosocial interventions tailored to the person's needs, to manage neurocognitive and functional symptoms, including the reduction of depressive and anxiety symptoms over years [5].

Combination antiretroviral therapy (cART) has dramatically reduced the risk of opportunistic central nervous system infection and severe dementia secondary to HIV infection in the past two decades, but HAND continues to have a significant impact on patients' quality of life [6].

Table 2 - Clinical-support characteristics and risk of dementia in HIV outpatients

Clinical/Support characteristics	Risk of dementia		*p* value	OR (95% CI)
	Low risk (n = 106)	High risk (n = 149)		
	median (IQI)	median (IQI)		
Time since HIV diagnosis (years)	11 (7.00-15.75)	12 (7.00-18.00)	0.67	1.00 (0.96-1.04)
DSSEmotional	4.00 (3.35-0.97)	3.83 (2.75-4.50)	0.040	0.78 (0.60-0.99)
DSSInstrumental	3.55 (2.60-4.57)	3.50 (2.70-4.50)	0.840	0.99 (0.79-1.23)
Global Severity Index	1.62 (1.38-2.31)	2.04 (1.55-2.68)	0.007	1.64 (1.12-2.43)
HIV Hospitalization	n (%)	n (%)		
No	77 (72.6)	113 (75.8)	0.66	1
Yes	29 (27.4)	36 (24.2)		0.84 (0.48-1.50)
Time ART initiation	n (%)	n (%)		
1	6 (5.7)	3 (2)	0.26	1
2	30 (28.3)	44 (29.5)		2.93 (0.71-14.76)
3	9 (8.5)	11 (7.4)		2.44 (0.49-14.32)
4	8 (7.5)	5 (3.4)		1.25 (0.21-8.13)
5	53 (50)	86 (57.7)		3.24 (0.82-15.89)
Adherence to therapeutic regime	n (%)	n (%)		
Yes	61 (57.5)	61 (41)	0.01	1
No	45 (42.5)	88 (59)		1.95 (1.18-3.25)
Hepatitis B infection	n (%)	n (%)		
No	90 (85)	122 (81.9)		1
Yes	6 (5.6)	19 (12.7)	0.09	2.33 (0.94-6.62)
Unknown	10 (9.4)	8 (5.4)		
Hepatitis C infection	n (%)	n (%)		
No	78 (73.6)	116 (77.8)		1
Yes	20 (18.9)	28 (18.8)	0.31	0.94 (0.49-1.80)
Unknown	8 (7.5)	5 (3.4)		
Presence of other diseases	n (%)	n (%)		
No	68 (64)	100 (67.1)	0.72	1
Yes	38 (36)	49 (32.9)		0.87 (0.52-1.48)
History of opportunistic disease	n (%)	n (%)		
No	85 (80.2)	110 (73.8)	0.30	1
Yes	21 (19.8)	39 (26.2)		1.43 (0.79-2.65)
People support	n (%)	n (%)		
1	50 (47.2)	78 (52.3)	0.71	1
2	2 (1.9)	4 (2.7)		1.28 (0.24-9.49)
3	6 (5.7)	8 (5.4)		0.85 (0.28-2.73)
4	43 (40.5)	56 (37.6)		0.83 (0.49-1.42)
5	5 (4.7)	3 (2)		0.38 (0.07-1.62)

Table 3 - Symptomatic characteristics and risk of dementia in HIV outpatients

	HAD			
	Low risk (n = 106)	**High risk** (n = 149)	*p* value	OR (95% CI)
Somatization, median (IQR)	1.50(0.85)	1.86(1.14)	0.06	1.41(0.98-2.06)
Obsessive_Compulsive, median (IQR)	1.83(0.83)	2.17(1.16)	0.003	1.75(1.22-2.55)
Interpersonal_Sensitivity, median (IQR)	1.50(1.00)	2.00(1.50)	0.02	1.49(1.11-2.05)
Depression, median (IQR)	1.83(1.17)	2.00(1.67)	0.06	1.30(0.98-1.74)
Anxiety, median (IQR)	1.83(1.00)	1.83(1.17)	0.09	1.31(0.95-1.84)
Hostility, median (IQR)	1.60(1.20)	2.00(1.20)	0.07	1.30(0.97-1.74)
Phobic_Anxiety, median (IQR)	1.40(1.00)	1.60(1.00)	0.10	1.27(0.92-1.77)
Paranoid_Ideation, median (IQR)	1.80(1.20)	2.20(1.20)	0.02	1.40(1.02-1.93)
Psychoticism, median (IQR)	1.80(1.15)	2.00(1.20)	0.04	1.45(1.04-2.02)

Although the widespread use of cART has prolonged the survival of people with HIV, the diagnosis of HIV-associated neurocognitive disorder (HAND) is essential in the long-term clinical management of the disease, and the identification of cognitive decline continues to be a clinical challenge [7]. Neurocognitive deficits remain a complex consequence of HIV infection. With a variable prevalence in different populations, even with treatment [7], the increase in the average life expectancy of these users for ages over 50 years is indicated as a risk factor by several authors, as a consequence of the decrease in the proliferation of T lymphocytes [8].

In this study, probable high risk of dementia among the participants was identified in 149 (58.4%) AIDS patients.

In univariate analysis, risk of dementia was not associated with sociodemographic variables at a significance level of 0.05. Our results differ from the results of Wubetu, Asefa & Gebregiorgis [9], where they

reveal that older participants had a 6% increase in the likelihood of a diagnosis of HIV-associated neurocognitive impairment compared to younger participants, OR 1.06 (95% CI = 1.03, 1.08) [9].

In our clinical and support analysis, we found that, among HIV patients, those who have better social support at the emotional level have a lower odds of dementia risk. Social support (emotional or instrumental) is a useful resource that helps minimize psychological stress and maladjusted reactions to the disease or limitations to adjust to it. It plays a key role in buffering the negative effects of HIV-related stigma [10]. Individuals may support patients living with HIV by remembering the medication time and can give material support.

We also observed that, among HIV patients, those who have a higher global severity index and those who did not adhere to the therapeutic regimen showed an increase of 64% and 95%, respectively, of having a high risk of dementia. Becker et al. [11], identified memory and learning deficits in adults with HIV and found that they were associated with low rates of adherence to the therapeutic regimen. The occurrence of neurocognitive disorders in HIV-positive patients may be due to non-adherence to treatment [3]. Low adherence to treatment also leads to an increase in viral load and a reduction in CD4 count [12]. GSI (psychological symptoms of distress) may raise the chance of non-adherence to the therapeutic regimen and impede its successful treatment and be connected with the disease's fast development and viral transmission.

Examined the nine subscales of depressive symptoms that comprised the global severity index, we observed that only four symptoms have a significant association with the high risk of dementia in patients with HIV. The odds of high risk of dementia in HIV patients increase as the degree of obsessive-compulsive symptoms increases OR 1.75 (CI 95% 1.22-2.55), interpersonal sensitivity OR 1.49 (CI 95% 1.11-2.05), paranoid ideation OR 1.40 (CI 95% 1.02-1.93) and psychoticism OR 1.45 (CI 95% 1.04-2.02).

In conclusion, patients with HIV with an association with the risk of dementia who have social support at the emotional level present a more favourable environment to control the disease and do not show deterioration of neurocognitive impairment.

Ethics committee and informed consent:

Ethical approval was granted from the Oporto School of Nursing Committee of Ethics. Participants were asked to sign an informed consent after being informed of the content and purpose of the study. Researchers did not interfere in any treatments or drugs administration. Data anonymity and confidentiality were guaranteed and the right to discontinue participation at any time during the study.

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