

# Motor impairments and predictors of mobility loss at the end of hospitalization in individuals with neurotoxoplasmosis

*Déficits motores e preditores de perda de mobilidade ao final da internação em indivíduos com neurotoxoplasmose*

*Déficits motores y predictores de pérdida de movilidad al final de la hospitalización en individuos con neurotoxoplasmosis*

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**ABSTRACT** | Neurotoxoplasmosis (NTX) is one of the main opportunistic diseases present in individuals with the human immunodeficiency virus (HIV). This disease promotes focal brain lesions with mass effect that can generate a variety of sequelae capable of compromising the performance of activities of daily living, including ambulation. Our study sought to verify the main motor deficits presented and identify risk factors for mobility loss at the end of hospitalization. It is an observational study, whose sample consisted of data from medical records of individuals with HIV and diagnosed with NTX. Electronic medical records were reviewed, clinical and epidemiological data were collected and hospital mobility was classified. Descriptive statistics and binary logistic regression were applied. We evaluated 161 medical records, with male prevalence, with a median age of 39 years. Motor deficits at admission were absence of ambulation (42.9%), hemiparesis (42.3%), lower limb paresis (37.3%), balance deficit (35.4%) and 32.9% could not walk at the end of hospitalization. Predictors of mobility loss at the end of hospitalization were: use of invasive mechanical ventilation (IMV), inclusion in the palliative care program and non-ambulation on admission. The main motor deficits were the absence of ambulation, hemiparesis on the right and the balance deficit. The predictors for inability to walk at the end of hospitalization were the need for IMV, inclusion in the palliative care program, and no ambulation at admission.

**Keywords** | Toxoplasmosis, Cerebral; HIV; Motor Disorders.

**RESUMO** | A neurotoxoplasmose (NTX) é uma das principais doenças oportunistas presentes em indivíduos portadores do vírus da imunodeficiência humana (HIV). A doença promove lesões cerebrais focais com efeito de massa que podem gerar uma variedade de sequelas capazes de comprometer a realização das atividades da vida diária, dentre elas, a deambulação. O objetivo deste estudo foi verificar os principais déficits motores apresentados e identificar os fatores de risco para a perda de mobilidade ao final da internação. Trata-se de um estudo observacional cuja amostra foi composta por dados de prontuários de indivíduos portadores do vírus HIV e diagnóstico de NTX. Foi realizada a revisão de prontuários eletrônicos e a classificação da mobilidade hospitalar, além da coleta de dados clínicos e epidemiológicos. Aplicou-se estatística descritiva e regressão logística binária. Foram avaliados 161 prontuários, com prevalência do sexo masculino e mediana de idade de 39 anos. Os déficits motores na admissão foram a ausência de deambulação (42,9%), hemiparesia (42,3%), paresia de membros inferiores (37,3%), déficit de equilíbrio (35,4%). Ao final da internação 32,9% não deambulavam. Os preditores para perda da mobilidade ao final da internação foram: utilização de ventilação mecânica invasiva (VMI), inclusão no programa de cuidados paliativos e não deambular na admissão. Os principais déficits motores foram a ausência de deambulação, a hemiparesia à direita e o déficit de equilíbrio.

**Descritores** | Toxoplasmose Cerebral; HIV; Transtornos Motores.

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**RESUMEN** | La neurotoxoplasmosis (NTX) es una de las principales enfermedades oportunistas presentes en individuos con el virus de la inmunodeficiencia humana (VIH). La enfermedad promueve lesiones cerebrales focales con efecto de masa que pueden generar una variedad de secuelas capaces de influir el desempeño de las actividades de la vida diaria, incluida la deambulaci3n. El objetivo de este estudio fue verificar los principales d3fcits motores presentados e identificar los factores de riesgo de p3rdida de movilidad al final de la hospitalizaci3n. Este es un estudio observacional cuya muestra consisti3 en datos de registros m3dicos de individuos con el virus del VIH y diagn3stico de NTX. Se revisaron los registros m3dicos electr3nicos y se clasific3 la movilidad hospitalaria, as3 como

la recolecci3n de datos cl3nicos y epidemiol3gicos. Se aplicaron estad3sticas descriptivas y regresi3n log3stica binaria. Evaluamos 161 registros m3dicos, con una prevalencia masculina y mediana de 39 a3os. Los d3fcits motores al ingreso fueron ausencia de deambulaci3n (42.9%), hemiparesia (42.3%), paresia de miembros inferiores (37.3%), d3fcit de equilibrio (35.4%). Al final de la hospitalizaci3n, el 32,9% no caminaba. Los predictores de p3rdida de movilidad al final de la hospitalizaci3n fueron: uso de ventilaci3n mec3nica invasiva (VMI), inclusi3n en el programa de cuidados paliativos y no deambulaci3n al ingreso. Los principales d3fcits motores fueron la ausencia de deambulaci3n, hemiparesia derecha y d3fcit de equilibrio.

**Palabras clave** | Toxoplasmosis Cerebral; VIH; Trastornos Motores.

## INTRODUCTION

Neurotoxoplasmosis (NTX) is one of the main opportunistic diseases present in individuals with HIV and AIDS (acquired human immunodeficiency syndrome), usually caused by the reactivation of a latent infection by *Toxoplasma gondii*<sup>1,2</sup>. NTX is the most common cause of expansive brain lesions with mass effect that can generate a variety of neurological sequelae, compromising functionality and performance of activities of daily living (ADL)<sup>3-5</sup>.

The clinical picture varies according to the topography and amount of brain lesions, and patients may present headache and insidious evolution of neurological alterations resulting of brain injuries, more frequently in the basal ganglia. Episodes of fever, intense headache (persistent and bilateral), seizures, altered consciousness level, hallucinations, speech and movement disorders may occur. Signs such as hemiparesis, dysphasia and other motor alterations are common due to the involvement of basal ganglia. Sensory-Motor alterations and postural balance impairing the ambulation<sup>2,6-8</sup> are also observed in these patients.

The loss of physical function and independence in ADL after a long period of hospitalization has been reported in the literature<sup>8,9</sup> and this decline is observed in HIV-positive patients, especially when associated with neurological disorders<sup>9</sup>. Hospitalization can cause loss of functional capacity, failure to recover prior deficits (cognitive deficit, presence of comorbidities, advanced age, low nutritional intake and severity of disease<sup>9</sup>) or even a continuous functional decline that increases institutionalization and death rates<sup>10,11</sup>.

Prevent mobility deficits during hospitalization is possible by working directly on modifiable risk factors. Identifying which risk factors aggravate mobility is necessary to promote preventive actions or recovery of these deficits<sup>11</sup>. Thus, the investigation of risk factors can minimize the negative consequences, favoring mobility and consequently improving the quality of life after hospitalization. No studies proposing an investigation of the risk factors that aggravate the mobility conditions during hospitalization were found in the literature. Given this context, our study pointed out the main motor deficits during hospitalization showed by patients with HIV and diagnosed with NTX, and verified the main predictors for mobility loss at the end of hospitalization.

## METHODOLOGY

An observational study conducted through the review of the data from electronic medical records of patients admitted between January 2015 and January 2017 in a tertiary-level hospital specialized in infecto-contagious and tropical diseases.

We selected medical records of patients that received clinical diagnosis of NTX after evaluation of the cranial tomography, positive result for HIV in the laboratory test, signs and symptoms of the disease, and recommended drug treatment with sulfadiazine, pyrimethamine, sulfamethoxazole folinic acid or trimethoprim. The medical records should contain the mobility classification described by the physical therapists. Initially, we intended to include medical records that contained the International Classification of Diseases (ICD); however, we decided

to ignore it due to the omission of this information in most of patients' records. Patients diagnosed with other diseases affecting the central nervous system (CNS) or ocular toxoplasmosis were excluded.

Patients' socio-epidemiological profiles were analyzed: age range, origin, naturalness, occupation, gender, life habits (smoking, alcoholism, use of illicit drugs), treatment with antiretroviral therapy (ART), laboratory and clinical variables such as viral load analysis (VL), TCD4 lymphocyte count (cluster of differentiation 4), polymerase chain reaction (PCR) for toxoplasmosis, immunoglobulin G (IgG) and M (IgM) serologies; headache, lowering of consciousness level, visual and speech alterations, seizures, fever and motor deficit. Moreover, surveys on patient's evolution in the physical therapy service were conducted to assess the mobility level. The service evaluates the patients using a mobility classification instrument described by Callen et al.<sup>12</sup>, translated into Portuguese and adopted by the service. The instrument classifies mobility into five levels according to the capabilities: (1) bed independence; (2) passive transfer; (3) active transfer; (4) assisted ambulation and (5) independent ambulation.

The data were treated as descriptive statistics, the continuous variables were showed in median and interquartile range, since the data did not have normal distribution, and the categorical variables in frequency and percentage. The identification of predictors of inability to ambulation at the end of hospitalization was obtained through the binary logistic regression test, using the estimates of the odds ratio, confidence interval (95%) and p value. The clinical and demographic variables considered as exposure factors and influencing the ability to walk at the end of hospitalization were included in the test.

We used the Statistical Package for the Social Science (SPSS) version 18.0 and considered a 5% significance level for statistical inference.

## RESULTS

We used 161 medical records, with an age variable with a median of 39 years and interquartile range from 33 to 46.5 years. Regarding gender, 99 (61.5%) were males, with elementary school as the predominant schooling level, with 60 patients (37.3%), and 67 (41.6%) were manual laborer. Table 1 shows the socio-epidemiological profile of patients with neurotoxoplasmosis of our study.

Table 1. Socio-epidemiological profile of patients with neurotoxoplasmosis

Variables	N	%
Gender		
Male	99	61.5
Female	62	38.5
Age groups		
18 – 30 years	23	14.3
30 – 50 years	115	71.4
50 – 70 years	22	13.7
> 70 years	1	0.6
Origin		
Capital city	59	36.6
Metropolitan region	40	24.9
Countryside	59	36.6
Other states	3	1.9
Naturalness		
Goiás	108	67
Others	53	33
Schooling level		
Illiterate	3	1.9
Elementary school	60	37.3
Medium	30	18.6
Higher Education	6	3.7
Ignored	62	38.5
Occupation		
Manual Laborer	67	41.6
Intellectual worker	17	10.5
Housewife/husband	31	19.3
Prisoner	4	2.5
Unemployed	2	1.2
Ignored	36	22.4
Not defined	4	2.5
Total	161	100

In total, 74 patients (46%) were smokers, 66 (41%) were alcoholic and 40 (25%) declared use of illicit drugs. At the hospital, the first choice treatment for NTX is a combination of sulfadiazine, pyrimethamine and folinic acid, lasting 6 weeks. Among the patients, 92,5% used this treatment; other patients used sulfamethoxazole folinic acid or trimethoprim. Regarding the use of ART, 125 (77.6%) patients were not using the therapy. Of this total, 65 (40.4%) patients were not using the therapy yet due to a recent diagnosis, 62 (38.5%) had abandoned treatment and 23 (14.3%) used the therapy in an irregularly. Regarding the TCD4 lymphocyte count, 67 (41.9%) patients had less than 50 cells, with a median of 44 cells/mm<sup>3</sup>,

with interquartile range of 22-109.25, while the viral load had a median of 22,9615 copies, with interquartile range of 34,606-575,765. The life habits and signs and symptoms presented on admission are shown in Table 2.

Table 2. Life habits, signs and symptoms presented on admission

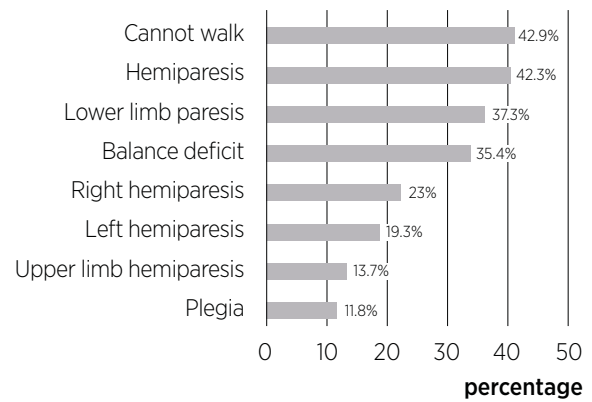
	N	%
Life habits		
Smoker	74	46
Alcoholic	66	41
Drug user	40	25
Treatment with ART		
Yes	36	22.4
No	125	77.6
Abandonment of ART	62	38.5
Recent diagnosis	63	39.1
Irregular use of ART	23	14.3
Signs and symptoms		
Headache	80	49.7
Motor deficit	138	85.7
Fever	63	39.1
LCL	94	58.4
Seizures	48	29.8
Visual alterations	29	18
Speech alterations	43	26.7

ART: antiretroviral therapy; LCL: Lowering of consciousness level.

The serological marker IgG for toxoplasmosis was positive in 59 cases (93.6%). IgM was positive in 2 cases (3.1%) among patients who underwent the exam (39.1%). The CRP test for *Toxoplasma gondii* on cerebrospinal fluid was positive in 55 samples (48.2%). Lumbar puncture was not performed in 47 patients (29.2%) due to medical contraindication. Only one patient underwent brain injury biopsy, with positive results for toxoplasmosis. Imaging exams suggested lesions due to toxoplasmosis in 94.4% of the cases.

The Glasgow coma scale was evaluated at admission, in which it was identified values from 3 to 8 in 20 cases (12.5%), 9 to 13 in 28 (17.5%) and from 14 to 15 in 113 patients (70%). The motor deficits found on hospital admission are described in Graph 1.

Regarding the mobility assessed by the instrument adopted in the service, which classifies mobility into five levels, we identified an improvement in mobility levels in the period between the admission and the outcome (discharge or death), as shown in Table 3. The inability to walk on admission was identified in 68 medical records (42.9%) and the outcome in 53 cases (32.9%).



Graph 1. Motor deficits present at hospital admission

Tabela 3. Mobility levels assessed at admission and hospital outcomes

Mobility	Admission		Hospital outcome	
	N	%	N	%
Level 1 - Bed restricted	48	29.8	39	24.2
Level 3 - Passive transfer	9	5.6	5	3.1
Level 3 - Active transfer	12	7.5	9	5.6
Level 4 - Assisted ambulation	40	24.8	48	29.8
Level 5 - Independent ambulation	52	32.3	60	37.3

The hospitalization period had a median of 23 days and interquartile range between 16 and 35.5 days. During hospitalization, 20 patients were included in the palliative care program (12.4%) and 45 required IMV (28%). The readmission rate (one and two readmissions) was 37.3%, and hospital mortality was 27.9%, considering the initial hospitalization and the readmissions. Physical therapy attendance was found in 126 medical records (78.3%) from admission to the outcome of hospitalization.

Table 4 shows the predictors identified for the inability to ambulation at the end of hospitalization were: use of IMV ( $p < 0.001$ ); inclusion in the end-of-life care program ( $p = 0.005$ ), which offers treatment with fewer invasive methods and iatrogenesis; and not to ambulate on admission ( $p < 0.001$ ).

Table 4. Predictive factors for mobility loss during hospitalization

	N (%)	OR	CI	p value
Do not ambulate on admission	68 (42.9)	9.729	2.850-33.216	<0.001
Use of IMV during hospitalization	45 (28)	19.985	5.321-75.069	<0.001
Palliative approach	20 (12.4)	16.858	2.338-121.574	<0.005

OR: odds ratio; CI: confidence interval; IMV: invasive mechanical ventilation.

## DISCUSSION

Despite the advances in controlling opportunistic diseases in patients with HIV/AIDS, especially after ART, the frequency and mortality related to these diseases remain high<sup>13</sup>. Galisteu et al.<sup>14</sup> also revealed that opportunistic diseases are frequent and consider that the discovery of their existence is especially related to the lack of adherence to the treatment, which was correlated to low schooling level. Our results also show low schooling level and non-adherence to the ART, especially when related to the recent diagnosis and treatment abandonment.

NTX was cited as the second most frequent opportunistic infection in HIV carriers, being directly related to the reduction of TCD4 lymphocytes. Moreover, having a viral load greater than 10,000 copies increases in 90% the chance of developing the disease<sup>14</sup>. We found low levels of TDC4 lymphocytes and high viral load in our study.

In the sample analyzed, the main signs identified were motor deficit, lowering of consciousness level and headache. Oliveira et al.<sup>15</sup> found that headache, strength deficit and fever were the most frequent symptoms in a group of patients with NTX. Right hemiparesis was the most reported motor deficit in this study, since it is greatly varied in the literature probably due to the diversity of sites and volume of brain lesions<sup>1</sup>.

Balance deficit, present in patients evaluated in our study, was also reported in another investigation with HIV/NTX patients. The authors related the balance deficit to hemiparesis, since this sequela generates neglect of the affected hemibody and loss of body perception, hindering ambulation<sup>8</sup>.

Despite the better life expectancy, it has been demonstrated that HIV patients have a decreased physical function when compared with non-infected people, which is not related to the degree of immunosuppression<sup>16</sup>. In our study, there was an improvement in mobility when compared hospital admission with outcome, which may be attributed both to the response to drug treatment and the early physiotherapeutic approach during the entire hospitalization.

Richert et al.<sup>17</sup> found a reduced functional capacity in HIV patients and a higher risk of falling. They considered that this reduction is not associated with the ART or CD4 count and viral load. In our study, these variables were also not related to mobility worsening and the inability to walk at the end of hospitalization. In a more recent study<sup>9</sup>, some factors were related to worse functional status: advanced age, presence of AIDS-related brain diseases

and diabetes. Among these factors, cerebral involvement was the most important factor for presenting a worse evaluation of functional performance.

The need for IMV during hospitalization was a predictor for non-ambulation, as described in studies conducted in intensive care units revealing that mechanically ventilated patients with prolonged hospitalization have higher risk of losing the ability to walk. Furthermore, 30 to 60 days of hospitalization increases by five times the risk of losing this motor ability<sup>8,18</sup> and, in our study, the hospitalization period was relatively long.

In general, HIV patients included in the palliative care program have greater clinical severity. This approach is often requested for terminally ill patients, which may justify their relationship with the absence of ambulation in hospital discharge<sup>19</sup>. Studies suggest that the palliative approach should be implemented in this public as early as possible and considers that this is essential in the care of the person living with HIV/AIDS<sup>20</sup>.

In our study, the inability to ambulate on hospital admission was verified in almost half of the medical records investigated, which may suggest that losing this ability abruptly makes the patient's recovery more difficult during hospitalization. Although there are no studies addressing this analysis in HIV carriers, a study with hospitalized older adults<sup>21</sup> found an association between low functionality at the end of hospitalization and the functional decline prior to admission, considering in-hospital mobility as a modifiable risk factor related to functional decline. The hospitalization process interferes substantially in functional capacity, especially after a critical disease, which may generate a significant decline in gait, sit-to-stand speed and strength, variables associated with the greatest dependence for daily activities<sup>22</sup>.

Although we observed improved mobility levels in medical records when compared hospital admission with outcome, based on our results, we could identify predictive factors of mobility reduction that can be used in clinical practice. This may have been discovered due to the proper drug approach and the early and comprehensive approach of physical therapy, which encourages patient's mobility and independence aiming at a better and faster recovery.

Study limitations are the intrinsic restrictions of retrospective investigations such as incomplete medical records or the absence of data. However, we emphasize the originality of the theme approached, since studies that performed this analysis in patients with HIV and diagnosed with NTX were not found in the scientific literature until the conclusion of our study.

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