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## CLINICAL AND EPIDEMIOLOGICAL ANALYSIS OF PATIENTS WITH HIV/AIDS ADMITTED TO A REFERENCE HOSPITAL IN THE NORTHEAST REGION OF BRAZIL

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### SUMMARY

The AIDS epidemic has become a worldwide phenomenon of enormous magnitude and extension, deeply transforming medical practices and public health initiatives. This retrospective survey aimed to analyze clinical and epidemiological characteristics of patients with HIV/AIDS admitted to the Institute of Tropical Diseases Natan Portella, Teresina, Piauí, Brazil, from January, 2001 through December, 2004. Of the 828 patients, 43% were from other states and 71.3% were men. Average patient age was  $35.4 \pm 11.5$  years-old and 85.5% were illiterate or had primary education. The main form of exposure to HIV was heterosexual behavior (54.1%), while injectable drug use was confirmed by only 2.7% of registered cases. The most frequent infectious complications were candidiasis (42.4%) and pneumocystosis (22.2%). Sixty-eight cases (8.2%) of visceral leishmaniasis were registered. Using multivariate analysis, individuals aged over 40 years-old, patients with active tuberculosis, *Pneumocystis carinii* pneumonia and central nervous system cryptococcosis showed increased risk of death. In this study, young male adults with low educational levels predominated and the most frequent opportunistic infections were candidiasis and pneumocystosis.

**KEYWORDS:** AIDS; Epidemiology; Opportunistic infections; Hospital mortality.

### INTRODUCTION

AIDS has become a global phenomenon of enormous magnitude and extension that has deeply transformed medical practice and public health initiatives<sup>30</sup>. Currently, an epidemiological transition is taking place, characterized by the dissemination of HIV/AIDS in smaller urban centers and among women, people of heterosexual orientation and lower socioeconomic status<sup>3,27</sup>.

One of the landmarks of the AIDS epidemiological profile consisted of the use of highly active antiretroviral therapy. Since then, the survival of individuals with HIV infection has increased and morbimortality rates have declined. The frequency of opportunistic infections affecting these patients has reduced and the variety has also changed<sup>23,25</sup>.

Despite the importance of this subject for understanding the amplitude of the HIV/AIDS epidemic, a lack of studies exists concerning this matter in the Northeast region of Brazil. The clinical and epidemiological characterization of this epidemic informs public health policies within the scope of developing prevention strategies, as well as setting the bases for medical assistance provided to infected patients<sup>5</sup>.

This survey aimed to study the epidemiological and clinical profile of HIV/AIDS patients admitted to the Institute of Tropical Diseases Natan Portella, emphasizing the main opportunistic infections and possible factors related to death.

### METHODS

The present research consisted of a retrospective study involving analysis of medical records. Patients with a diagnosis of HIV/AIDS admitted to the Institute of Tropical Diseases Natan Portella (*Instituto de Doenças Tropicais Natan Portella*, IDTNP) from January, 2001 through December, 2004 were included in the study. The IDTNP is a tertiary center of regional reference and also a teaching hospital of the Federal University of Piauí, which polarizes the attendance of infectious-contagious diseases in the state of Piauí, Brazil, and nearby states. It is located in Teresina, the state capital, which has a population of 748,336 inhabitants and is an important reference in health services in Northeast Brazil.

The study was realized by a protocol based in the following items: date of the initial attendance at the IDTNP, gender, age, educational level, occupation, patient's city of residence, civil status, race, religion, probable mode of HIV acquisition, number of lymphocytes CD4/mm<sup>3</sup>, CD8/mm<sup>3</sup> and relation CD4/CD8 on the occasion of the initial attendance, type and number of the most frequent infections during clinical follow-up, number and duration of hospitalizations in the period studied, date of death and number of diagnosed infectious complications in the patients who died.

The categories of HIV exposure were adopted from the epidemiological surveillance system of Brazil's Ministry of Health, known as the System of Information of Illnesses and Notification (*Sistema de*

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*Informação de Agravos de Notificação*, SINAN), relative to AIDS. The enclosed categories were: 1) “male homosexuals”, 2) “bisexuals”, 3) “heterosexuals”, 4) “injectable drug use” (IDU), 5) “blood transfusion”, 6) “vertical transmission”, 7) “accident with biological material”, 8) “hemophilia” and 9) “ignored”. In categories 1, 2 and 3, previous history of sexual relations with multiple partners or with HIV-positive individuals was also investigated. In the IDU category, individuals who answered positively were included, independent of their sexual orientation.

A diagnosis of HIV infection was realized using the current norms of Brazil’s Ministry of Health<sup>18,20</sup>. Two positive samples of ELISA (Enzyme-linked Immunosorbent Assay) for anti-HIV 1 or 2 antibodies were then confirmed by Western-blot method, which was considered positive when both core and envelope bands (p24 and gp120/160 or gp41) were present.

The diagnosis of opportunistic diseases and other complications was performed according to clinical criteria, complementary exams routinely performed in the IDTNP and favorable therapeutic response to each specific condition. A diagnosis of *Pneumocystis carinii* pneumonia (PCP) was supported by response to the treatment with trimethoprim-sulfamethoxazole and compatible clinical and radiological status. Tuberculosis (TB) was diagnosed on the basis of a positive bacilloscopy for Ziehl-Nielsen staining or identification of the agent in tissue or sputum culture when clinical and radiological exams elicited suspicion. Symptom resolution with rifampin, pyrazinamide and isoniazid treatment or suggestive histopathological findings were also considered for TB diagnosis. Cerebral toxoplasmosis was considered in the presence of typical signs and convincing symptoms, alterations in computerized tomography and/or magnetic resonance image, positive serology for *Toxoplasma gondii* and clinical improvement with sulfadiazine and pyrimethamine. The diagnosis of cryptococcosis was sustained by the following aspects: suggestive neurological status, lumbar puncture with cerebrospinal fluid samples revealing positive China ink and clinical improvement with an antifungal scheme. Autopsy was not performed on patients who died.

The present study was approved by the Committee of Ethics in Research at the Federal University of Piauí (UFPI) and at the Institute of Tropical Diseases Natan Portella (IDTNP).

**Statistical analysis:** The results were analyzed by statistical programs SPSS 13.0 for Windows and MedCalc Version 9.3.2.0. Univariate analysis was performed to assess the association between death and categorized risk factors. Adjusted odds ratio [OR] and 95% confidence intervals were estimated. The significance of measurement was determined by Chi-square ( $\chi^2$ ) and Fisher exact tests. Finally, a multivariate analysis using logistic regression was performed in order to check for possible confounding variables. Lost data was excluded from the analysis. A value of  $p \leq 0.05$  was considered as statistically significant.

## RESULTS

A total of 919 medical records were reviewed in the study, however 91 were excluded due to insufficient data or inconclusive diagnosis. Of the 828 patients studied, the average age was  $35.4 \pm 11.5$  years and men were the most prevalent (71.3%). The demographic and behavioral data of the patients can be verified in Tables 1 and 2.

**Table 1**  
Demographic characteristics of patients admitted to the Institute of Tropical Diseases Natan Portella, Piauí State, Brazil

Demographic characteristics	No./No. of patients	Percentage (%)
Age, mean $\pm$ SD years	35.4 $\pm$ 11.5 (16 days - 78 years)	
Gender		
Male	590/828	71.3
Female	238/828	28.7
M : F	2.48 : 1	
Race		
White	52/824	6.3
Black	12/824	1.5
Mixed	760/824	92.2
Education		
None	94/827	11.4
Primary	613/827	74.1
Secondary	84/827	10.2
Tertiary	21/827	2.5
Not applied	15/827	1.8
Civil status		
Married	252/827	30.5
Single	475/827	57.4
Steady union	53/827	6.4
Widower	27/827	3.3
Not applied	20/827	2.4
Place of residence		
Teresina	264/828	31.9
Interior of Piauí	208/828	25.1
Other States	356/828	43.0
Residence area		
Urban	712/827	86.1
Rural	115/827	13.9
Occupation		
Home maker	169/827	20.4
Farm worker	140/827	16.9
Student	73/827	8.8
Construction worker	30/827	3.6
Not applied	19/827	2.3
Others	396/827	48.0
Religion		
Catholic	773/818	94.5
Protestant	25/818	3.1
Umbandist	18/818	2.2
Others	2/818	0.2

**Table 2**

Epidemiologic and behavioral characteristics associated with the acquisition of HIV infection among patients admitted to the Institute of Tropical Diseases Natan Portella, Piauí State, Brazil

Risk factors	No./No. of patients	Percentage (%)
<b>Sexual orientation</b>		
Homosexual	52/638	8.1
Heterosexual	345/638	54.1
Bisexual	113/638	17.7
Not applied	19/638	3.0
Ignored	109/638	17.1
<b>Sexual relation with multiple partners</b>		
Yes	284/637	44.6
No	103/637	16.2
Ignored	250/637	39.2
<b>Sexual contact with HIV infected individuals</b>		
Yes	49/638	7.7
No	207/638	48.1
Ignored	282/638	44.2
<b>Injectable drug use</b>		
Yes	17/639	2.7
No	514/639	80.4
Ignored	108/639	16.9
<b>History of blood or derivative transfusion</b>		
Yes	18/638	2.8
No	533/638	83.5
Ignored	87/638	13.6
<b>Vertical transmission</b>		
Yes	11/638	1.7
No	83/638	13.0
Not applied	165/638	25.9
Ignored	379/638	59.4

The initial CD4<sup>+</sup> lymphocyte counts were located in 353 medical archives. Fourteen patients (4%) presented more than 500 cells/mm<sup>3</sup>; in 73 (20.7%) the count was between 200 and 500 cells/mm<sup>3</sup> and 266 (75.4%) presented less than 200 cells/mm<sup>3</sup>.

During the clinical course, 798 (96.4%) patients required up to four hospitalizations in the IDTNP and 582 (70.4%) were admitted for up to 30 days. In 789 patients (95.3%), up to four infectious complications were present. The main opportunistic infections were candidiasis (42.4%) and *Pneumocystis carinii* pneumonia (22.2%) (Table 3). Diarrhea

was a complication observed in 429 (51.8%) patients, 100 (39.4%) of whom presented diarrhea at death. Other opportunistic infections, such as staphylococci, scabies, herpes simplex, herpes zoster, bacterial meningitis, nonspecific pneumonia, urinary infection, cryptosporidiosis, syphilis, cytomegalovirus, American tegumentary leishmaniasis, neurocysticercosis, showed individual frequencies of lower than 16 cases (3.5%).

Of the 828 patients investigated, 254 died (30.7%) and of these, 194 (76.4%) died during the initial attendance and 44 (17.3%) within the first 48 h of hospitalization. The average number of admittances per patient was 1.5 ± 1.4 (1-15). The number of infectious complications at death was of 2.1 ± 1.1 (0-8) and 231 (90.9%) patients presented up to three opportunistic infections at death. The most prevalent opportunistic infections were: candidiasis (37.8%), PCP (33.5%) and active tuberculosis (23.2%) (Table 3).

Using univariate analysis, individuals aged over 40 years-old ( $p = 0.020$ ), patients with active tuberculosis ( $p = 0.001$ ), *Pneumocystis carinii* pneumonia ( $p = 0.001$ ) and central nervous system cryptococcosis ( $p = 0.001$ ) were associated with more severe clinical outcomes and increased risk of death. No significant interactions were found between gender, residential area, educational levels, more than three opportunistic infections, CD4 count, neurotoxoplasmosis, visceral leishmaniasis, bacterial pneumonia, sexual contact with an HIV-infected individual and injectable drug use with the risk of a fatal outcome. In the final logistic regression analysis, age, patients with active tuberculosis, PCP and central nervous system cryptococcosis were significantly associated with a fatal outcome (Table 4).

## DISCUSSION

This survey consisted of a retrospective analysis of data collected from medical records, which is less reliable than prospective, randomized and controlled studies<sup>16</sup>. The main difficulties observed were: incomplete medical records and/or the absence of necessary information, which led to exclusion; a lack of standardization of certain medical routines; and the possibility of spontaneous clinical remission or improvement, which could have been erroneously attributed to the type of treatment provided. Nevertheless, this study was realized in a public center of regional reference in infectious and parasitic diseases. Thus, individuals taken care of in private hospitals were not included, which could cause disagreement with the HIV/AIDS epidemic trends in the general population. Despite these limitations, this is a pioneer study in the Northeast region of Brazil, correlating demographic, epidemiological and clinical characteristics of patients presenting HIV/AIDS. Moreover, we believe that the results reflect the reality of medical attendance in the environment where the IDTNP is inserted.

An important epidemiological impact of the present study was also observed when compared to the AIDS epidemic in Piauí State. In fact, the group of patients who lived in Piauí admitted to the IDTNP from 2001 through 2004 represented 28.5% of the total number of cases notified in Piauí State up to 2004 (1,655 cases). However, if patients from the capital Teresina are considered individually, a similar proportion is maintained (264 out of 1,000 cases)<sup>19</sup>. Although the majority of patients lived in Piauí State, almost half came from other States, especially Maranhão. This brings up the hypothesis of a scarcity of specialized centers, as well as a

**Table 3**  
Main opportunistic infections among patients admitted to the Institute of Tropical Diseases Natan Portella, Piauí State, Brazil

Opportunistic infections	All patients		Death occasion	
	No./ No. of patients	%	No./No. of patients	%
Candidiasis	351/828	42.4	96/254	37.8
Oral	326/828	39.4	88/254	34.6
Esophageal	47/828	5.7	10/254	3.9
Pulmonary	1/828	0.1	-	-
Vaginal	2/828	0.2	-	-
Ocular	1/828	0.1	-	-
Disseminated	1/828	0.1	1/254	0.1
<i>Pneumocystis carinii</i> pneumonia	184/828	22.2	85/254	33.5
Bacterial pneumonia	173/828	20.9	44/254	17.3
Toxoplasmosis	179/828	20.1	50/254	19.7
Cerebral toxoplasmosis	164/828	19.8	50/254	19.7
Ocular toxoplasmosis	5/828	0.6	-	-
Tuberculosis	141/828	17.0	59/254	23.2
Pulmonary	126/828	15.2	55/254	21.7
Ganglionic	21/828	2.5	1/254	0.4
Cerebral	3/828	0.4	3/254	1.2
Visceral leishmaniasis (Kalazar)	68/828	8.2	19/254	7.5
Sepsis	30/828	3.6	19/254	7.5
<i>Cryptococcus</i> sp.	31/828	3.6	20/254	7.9
Pulmonary cryptococcosis	3/828	0.3	1/254	0.4
Cerebral cryptococcosis	28/828	3.4	19/254	7.5

**Table 4**  
Variables associated with a fatal outcome among patients admitted to the Institute of Tropical Diseases Natan Portella, Piauí State, Brazil

Factor	Odds Ratio (95% Confidence Interval)	Adjusted <i>p</i> value
Aged more than 40 years-old	1.64 (1.72 - 2.28)	<i>p</i> = 0.004
Active tuberculosis	2.30 (1.55 - 3.41)	<i>p</i> < 0.0001
<i>Pneumocystis carinii</i> pneumonia	3.17 (2.22 - 4.53)	<i>p</i> < 0.0001
Cryptococcosis	9.22 (3.91 - 21.78)	<i>p</i> < 0.0001

possible preference of the patients to receive treatment far from their home towns for reasons of privacy<sup>29</sup>. It is valid to point out that 36.35% were from cities of less than 50,000 inhabitants and 13.9% of the patients came from rural areas. This reflects the interiorization and ruralization trend of the AIDS epidemic and its spread beyond large urban centers<sup>15</sup>.

The patients studied presented a low educational level and nonqualified occupations. Education and occupation are used as socioeconomic indicators of patients with AIDS and more recent studies have signaled the impoverishment of the epidemic population<sup>27,14</sup>. However, it should be highlighted that few individuals with higher socioeconomic status were admitted to the IDTNP service; even though this is a public center of regional reference in infectious and parasitic diseases.

Young adults and male gender predominated in this research. The rate between men and women was 2.5:1 (M:W), which is in agreement with the current trend of epidemic dissemination among women<sup>24</sup>. The low M:W rate obtained can be partially explained by sexual exposure as the most probable form of HIV transmission, with prominence of heterosexual behavior. The increase in heterosexual cases is a decisive factor concerning the increased female participation in the epidemic<sup>9,11,12</sup>. These data reflect the importance of interrupting the epidemiological chain that is occurring in our region, through preventive policies focusing on female participation in the epidemic. It is undeniable that this study illustrates a picture of the epidemic's course at a local level, although future research involving not only hospitalized patients, but all registered AIDS notifications, are still

required to obtain a clearer idea of the actual extent of the phenomenon observed at the present time.

Homosexual/bisexual exposure corresponded to 25.1% of the patients. It is interesting to note that nearby States, such as Pernambuco and Ceará, have presented higher levels of homosexual-bisexual exposure (39%)<sup>27</sup>. This was an important characteristic at the onset of the epidemic, which differs from contemporary data. Even so, underreporting of these cases may be occurring, since bisexual behavior can frequently be hidden by cultural issues, due to this group's tendency of only stating its heterosexuality<sup>26</sup>.

Regarding blood exposure, 18 patients referred to previous history of blood transfusion, reflecting rigid blood bank and hemoderivative control. Injectable drug use (IDU) is not an important via of exposure in the North and Northeast regions of Brazil, a fact confirmed by only 17 registered cases in the IDTNP. Other authors have reported a high rate of IDU in the Southeast region, supplanting heterosexual exposure<sup>3,11</sup>.

Of the 828 patients included in the present study, 638 (77%) notifications were located in SINAN. The underreporting of HIV/AIDS cases occurs mainly due to a lack of attention to the requirement for notification and/or errors in data collection and documentation. FERREIRA & PORTELA<sup>10</sup> affirmed 42.7% underreporting in the city of Rio de Janeiro, in which the lower values occurred in patients admitted to university hospitals and federal institutions with their own funding. The IDTNP is classified as a hospital-school, where both research and medical residences are established, which justifies the low level of underreporting. However, this rate is still high when compared to countries with superior availability of research funds and directed campaigns aimed at the importance of notification<sup>2,4</sup>.

The most common complication was nonspecific diarrhea, an expressively large proportion when compared to other centers<sup>11</sup>. Few patients underwent stool parasitological exam or investigation for cryptosporidium, *Isospora belli* or microsporidia on stool samples. Moreover, stool culture is not an exam routinely performed in this center. Such issues could explain the low rate of 10 (1.2%) cryptosporidiosis cases registered among these patients. Despite this, studies linking AIDS and diarrhea that lead to an extensive etiological inquiry, including viral agents, have found the incriminating pathogen in the majority of cases<sup>13,31</sup>. Reports in the literature, allied with a favorable response to support therapy and antimicrobials in the patients of the present study, reinforces the hypothesis that most diarrhea cases had infectious etiology.

A large number of cases of *Pneumocystis carinii* pneumonia were verified (22.2%), in contrast with other studies that show a reduction in PCP frequency in the post-HAART era<sup>11,23</sup>. Furthermore, various studies indicate a strong correlation of hospitalization due to PCP with: 1) a lack of health assistance or 2) absence of knowledge of HIV infection status by the patient<sup>1</sup>. These conditions are overlapped, respectively, with the remote location of the patient's residence and low educational level of the majority of the individuals admitted to the IDTNP<sup>17</sup>.

The registered cases of active tuberculosis were lower than those reported in the medical literature<sup>22,23</sup>. In a series of 135 patients in India, this was the most common opportunistic infection, present in 71.1% of patients<sup>29</sup>. In contrast, TB/HIV coinfection was detected in 23.2%

of the patients who died in the IDTNP. This scenario raises reflections concerning the possible delayed diagnosis of TB/HIV coinfection and/or misdiagnosis.

Visceral leishmaniasis (VL) was another infection of impact in this study. VL is considered an emerging infectious disease in different Brazilian urban areas. In the state of Piauí, VL has been recognized since 1934 and in 1980, it spread as an epidemic of enormous extension that was concentrated in Teresina. Today, this city is considered one of the main urban foci of the disease in Brazil<sup>6,7,8</sup>. Among patients with AIDS hospitalized in the IDTNP, 68 cases (8.2%) of VL were registered, all from endemic areas, expressively from Piauí and Maranhão States. AIDS-VL coinfection is well documented and varies from 1.5% to 9% in patients with AIDS in endemic areas of VL<sup>29</sup>. Campaigns directed at combating the vector insect and reservoir control are of extreme necessity. Early diagnosis is essential to reduce HIV/VL lethality by establishing efficient therapeutic and prophylactic measures<sup>21</sup>.

Individuals aged over 40 years-old, tuberculosis infection, *Pneumocystis carinii* pneumonia and cryptococcosis of the central nervous system are all associated with more severe clinical outcomes and consequent evolution to death. A study realized by SACKOFF *et al.*, of patients registered in New York City, showed an increased rate of mortality for causes related to HIV with advanced age (greater than 65 years) and in women<sup>28</sup>.

In conclusion, a large number of patients from home cities other than Teresina and low educational level could justify a lack of adherence to antiretroviral therapy and/or prophylaxis of opportunistic diseases. Therefore, opportunistic infections remain frequent even in the post-HAART era in populations where access to healthcare is limited. Therefore, it is essential to create new specialized centers to provide care for HIV patients and to distribute antiretroviral medication. In addition, ample qualification of health professionals, aimed at early recognition and adequate management of AIDS, is an important measure for the survival of patients that suffer from this condition.

## RESUMO

### Análise clínica e epidemiológica dos pacientes com HIV/AIDS internados em um Hospital de Referência na Região Nordeste do Brasil

A epidemia de AIDS tornou-se um fenômeno mundial de grande magnitude e extensão, transformando profundamente a prática médica e as iniciativas em saúde pública. O estudo retrospectivo analisou as características clínicas e epidemiológicas dos pacientes com HIV/AIDS internados no Instituto de Doenças Tropicais Natan Portella, Teresina, Piauí, Brasil, de janeiro de 2001 a dezembro de 2004. Dos 828 pacientes, 43% eram provenientes de outros estados e 71,3% eram do sexo masculino. A idade média foi 35,4 ± 11,5 anos. Eram analfabetos ou cursaram até o ensino fundamental 85,5%. A principal via de exposição ao HIV foi o comportamento heterossexual (54,1%), enquanto o uso de drogas injetáveis foi observado em apenas 2,7% dos casos registrados. As complicações infecciosas mais frequentes foram candidíase (42,4%) e pneumocistose (22,2%). Foram computados 68 casos de leishmaniose visceral. Em análise multivariada, idade acima de 40 anos, portadores de tuberculose, pneumonia por *Pneumocystis carinii*,

neurocriptococose associaram-se a maior risco de evolução para o óbito. Predominaram, neste estudo, adultos jovens do sexo masculino, com baixa escolaridade, tendo como infecções oportunistas mais frequentes candidíase e pneumocistose.

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