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Characterisation and variables associated with mortality in a population with HIV and central nervous system opportunistic infections in a Colombian public hospital in Bogotá


Facultad de Medicina, Posgrado de Neurología, Universidad de La Sabana, Chía, Cundinamarca, Colombia
Servicio de Neurología, Subred de servicios de salud suroccidente, Bogotá, Colombia

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Abstract

Introduction: HIV-associated mortality after a central nervous system opportunistic infection can reach up to 78%. In populations with limited economic resources, few studies have evaluated the clinical outcomes of these infections in patients with HIV.

Methods: We performed an observational analytical study using our hospital’s database. Sociodemographic, clinical, and paraclinical data were gathered from patients with HIV-associated opportunistic neurological infections attended between January 2019 and January 2021. The aim of the study was to describe the in-hospital mortality rate and to establish associations with sociodemographic, clinical, and paraclinical variables.

Results: Seventy-five patients were included, with a mean age of 38.7 years. Fourteen (31.8%) were receiving antiretroviral therapy at the time of admission. The most frequent neurological infections were cerebral toxoplasmosis (37.3%, n = 28), meningeal cryptococcosis (20%, n = 15), and neurosyphilis (20%, n = 15). The in-hospital mortality rate was 25.3% (n = 19). The variables associated with increased mortality risk were diagnosis of meningeal cryptococcosis, admission to the ICU, and presence of fever. The variables associated with decreased mortality risk were CSF/blood glucose ratio > 0.5 and normal body mass index (18–25).

Conclusions: In a population of patients with HIV-associated opportunistic neurological infections, in-hospital mortality was 25.3%. The diagnosis of meningeal cryptococcosis, admission to the ICU, and the presence of fever are associated with higher mortality risk. To the contrary, CSF/blood glucose ratio > 0.5 and normal body mass index are associated with lower mortality risk.

Abbreviations: BUN, blood urea nitrogen; IL, interleukin; CSF, cerebrospinal fluid; CRP, C-reactive protein; AIDS, acquired immune deficiency syndrome; CNS, central nervous system; ART, antiretroviral therapy; ICU, intensive care unit; HIV, human immunodeficiency virus; BMI, body mass index

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Caracterización y factores asociados con mortalidad en población con VIH y neuroinfección oportunistas en un hospital público en Bogotá, Colombia

Resumen

Introducción: La mortalidad asociada al VIH luego de una infección oportuna del SNC puede ser hasta del 78%. En poblaciones de bajos recursos económicos, existen pocos estudios que evalúan el desenlace clínico de estas infecciones en pacientes con VIH.

Metodología: Estudio observacional analítico usando la base de datos del hospital base de los investigadores. Se extrajeron datos sociodemográficos, clínicos y paraclinicos de los pacientes con neuroinfecciones oportunistas asociadas a VIH, entre enero del 2019 y enero del 2021. Se busca describir la mortalidad al final de la hospitalización y establecer asociaciones con las variables sociodemográficas, clínicas y paraclinicas.

Resultados: Se incluyeron 75 pacientes. La edad media fue 38.7 años. El 31.8% (n = 14) estaba recibiendo terapia anti-retroviral al momento del ingreso. Las neuroinfecciones más frecuentes fueron toxoplasmosis cerebral (37.3%, n = 28), criptococosis meníngea (20%, n = 15) y neurosifilis (20%, n = 15). La mortalidad al final de la hospitalización fue de 25.3% (n = 19).

Conclusiones: En una población de pacientes con neuroinfección oportuna asociada a VIH, la mortalidad al final de la hospitalización fue de 25.3%. El diagnóstico de criptococosis meníngea, ingreso a UCI y presencia de fiebre. Las variables asociadas con disminución del riesgo de mortalidad fueron: relación de glucorraquia/glucemia mayor de 0.5 e IMC normal (18–25).

Abreviaturas

<table>
<thead>
<tr>
<th>Abreviatura</th>
<th>Definición</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN</td>
<td>nitrógeno ureico</td>
</tr>
<tr>
<td>IL</td>
<td>interleucina</td>
</tr>
<tr>
<td>LCR</td>
<td>líquido cefalorraquideo</td>
</tr>
<tr>
<td>PCR</td>
<td>proteína C reactiva</td>
</tr>
<tr>
<td>SIDA</td>
<td>síndrome de inmunodeficiencia adquirida</td>
</tr>
<tr>
<td>SNC</td>
<td>sistema nervioso central</td>
</tr>
<tr>
<td>TAR</td>
<td>terapia antirretroviral</td>
</tr>
<tr>
<td>UCI</td>
<td>unidad de cuidado intensivo</td>
</tr>
<tr>
<td>VIH</td>
<td>virus de inmunodeficiencia humana</td>
</tr>
<tr>
<td>IMC</td>
<td>índice de masa corporal</td>
</tr>
</tbody>
</table>

Introduction

In 2020, approximately 38 million people worldwide had human immunodeficiency virus (HIV) infection, and circa 1.5 million people were infected de novo; a total of 680,000 HIV-related deaths were recorded that year. In Colombia, the prevalence of HIV has increased over time, with 120,000 patients in 2010 and approximately 180,000 in 2020. In 2021, 14,698 new cases were reported; 11.3% of these cases presented opportunistic infections, with 0.8% corresponding to cerebral toxoplasmosis.1,2

Central nervous system (CNS) involvement secondary to some opportunistic infection is estimated to constitute the initial symptom in 10%–20% of patients. Furthermore, these infections define the AIDS stage and are associated with a high risk of mortality, with rates close to 50%.4 The pathogenic agents vary according to geographical region. The most frequent infections in Latin America are cerebral toxoplasmosis, tuberculosis meningitis, and cryptococcal meningitis, whereas in North America and Europe, the most frequent are progressive multifocal leukoencephalopathy, toxoplasma encephalitis, and cryptococcal meningitis.5

Since the introduction of antiretroviral therapy (ART), changes have been observed in the manifestation of neurological infections, with an increased age of onset and higher CD4 T lymphocyte counts at the time of diagnosis.4 However, it has been reported that only 6.8% of patients with HIV-associated CNS opportunistic infections present virological suppression.9 Furthermore, low CD4 T lymphocyte counts, high viral loads, and the lack of ART are associated with poorer prognosis, directly related to the higher risk of opportunistic infections.6,7 Independently of the administration of ART, the factors influencing infection...
with opportunistic pathogens include lack of knowledge of the
stage of the disease, resistance to ART, poor treatment
adherence, and the use of intravenous drugs that may
interfere with medication pharmacokinetics.6,7

Some sociodemographic factors have been shown to
increase the risk of HIV infection, while also influencing
the course and outcomes of the disease. For instance,
people with limited socioeconomic resources have been
shown to present higher prevalence of HIV/AIDS and higher
mortality rates.8 The opportunistic infection associated with
the highest mortality rate is cryptococcosis, followed by
Pneumocystis jirovecii pneumonia, regardless of the age of
diagnosis with HIV infection, sex, ethnicity, CD4 T lympho-
cyte count, ART, transmission category, antibiotic prophyl-
axis, method of HIV infection, or development of other
opportunistic infections.9

Despite the existence of ART, CNS infections have a
significant impact on outcomes in patients with HIV
infection, and therefore they remain a challenge for those
physicians treating these infections. Few studies have been
published in Latin American countries or populations with
limited economic resources on the form of presentation and
the variables associated with poorer prognosis. We con-
ducted a study at a tertiary-level public hospital in Bogotá
(Colombia) that serves a population of approximately 2.5
million people living in the south-west of the city. In 2017,
8.5–21.2% of the population lived in poverty, with 3.4–
4.9% living in extreme poverty.9 In our region, the rate of
reported cases of HIV infection was 40.3–55.8/100000
population in 2019, and 41.4–56.4/100000 population in
2021; the mortality rate amounted to 2.4–4.4/100000
population in 2019 and 3.8–5.9/100000 population in 2021.10

It is important to determine the clinical and paraclinical
characteristics of these patients to develop new strategies
that may enable differential approaches with a positive
impact on clinical outcomes. The aim of this study is to
describe the clinical and paraclinical variables associated
with in-hospital mortality among patients with a diagnosis of
HIV-associated neurological infection attended at Hospital
de Kennedy in Bogotá (Colombia), during the period
between January 2019 and January 2021.

Methods

Study design and patient selection

We used the hospital database to conduct a retrospective
study. We collected basic sociodemographic data, time from
symptom onset to consultation, symptoms leading to
consultation, the neurological infection diagnosed, HIV
diagnostic status at the time of admission, use of ART,
serum and cerebrospinal fluid (CSF) laboratory findings,
head CT scan findings, intensive care unit (ICU) admission,
duration of hospitalisation, concomitant infections outside
the CNS, and outcome, defined as survival or death during
hospitalisation. In this study, abnormal CT results were
defined as presence of space-occupying lesions, with the
remaining findings considered normal.

We selected these variables because they are usually
described in CNS infections, and may have an impact on the
prognosis and outcomes of these patients.10,11 Some have
been associated with a higher mortality rate specifically in
populations with HIV infection, but have not been assessed
in our population.4,5,12

Inclusion criteria were admission between January 2019
and January 2021, and diagnosis of HIV-associated CNS
opportunistic infection. We excluded patients for whom
information on outcomes was not available. The study was
evaluated and approved by our hospital’s ethics committee.

Statistical analysis

We performed a basic descriptive statistical analysis of the
variables included. We calculated frequencies and percent-
ages for categorical variables, and means and standard
deviations for continuous variables. The minimum and
maximum values were considered when relevant. The
outcome was defined as the dichotomous dependent
variable (death or survival). We performed a univariate
analysis of the selected clinical and paraclinical variables.
We used logistic regression to calculate odds ratios both for
continuous and for categorical variables. We also calculated
the confidence intervals and P-values. We established an
alpha coefficient of 0.05 for statistical significance. All
calculations were performed with version 16.1 of the Stata
software.

Results

We included a total of 75 individuals. Mean age was
38.7 years, and the majority were men (Table 1). Of the
total sample, 6 belonged to a special population: 5
intravenous drug users and one rough sleeper. The most
frequent diagnosis was toxoplasmosis, in 37% of patients,
followed by neurosyphilis and cryptococcosis, in 20% each,
opportunistic neurological infection in 13%, and meningial
tuberculosis in 9%. The other infections were bacterial
meningitis (3 patients), fungal infection other than with
Cryptococcus (2 patients), herpes encephalitis (1 patient),
coinfection with cryptococcosis and meningeal tuberculosis
(1 patient), coinfection with neurosyphilis and cytomegalov-
irus (1 patient), coinfection with toxoplasmosis and
cryptococcosis (1 patient), and neurological infection of
undetermined cause in 1 patient. The most frequent
symptom at admission was headache, in 64% of cases,
followed by fever in 40% and altered level of consciousness
in 24% (Table 1). HIV infection had been diagnosed
previously in 58.7% of patients, with only 31% receiving
ART. Twenty-five percent were admitted to the ICU. Mean
hospital stay was 28.4 days, and 25% of patients died during
admission.

Of the 69 patients for whom data were available on CD4 T
lymphocyte count, 76% presented levels below 200 cells/
mm³, with a mean count of 102 cells/mm³. Fifty-eight (77%)
patients underwent a lumbar puncture. Mean CSF opening
pressure was 22.8 cm H₂O (normal range: 6–25); 55%
presented normal glucose levels (> 50 mg/dL), although
approximately 61% showed a CSF/blood glucose ratio < 0.5.
Sixty-four percent presented elevated CSF protein level
(>45 mg/dL), with 38% displaying pleocytosis. Table 2 shows
the blood, CSF, and cranial CT scan findings.
Fever is reported to be correlated with a presence of fever is reported to be correlated with a presence of fever. This may support our findings, which revealed 5.25 times greater mortality risk by up to 50% if the infection is not adequately treated within the first 48 h.14 Presence of fever is reported to be correlated with a lower mortality rate in patients with fever at admission (P = .02), diagnosis of meningeal cryptoccocosis (P = .02), and admission to the ICU (P = .004). We also observed that mortality risk increased by 1.28 times for every 1000 neutrophils in the blood count (P = .015) and by 1.14 times for every increment of mg/dL in blood urea nitrogen (BUN) (P = .003) (Table 3).

Additionally, we observed a decrease in mortality risk associated with each 10 cell/μL increment in the CD4 T lymphocyte count (P = .02), with CSF/blood glucose ratios above 0.5 (P = .07), and with BMI within normal ranges (18–25) (P = .03) (Table 3).

### Discussion

In a vulnerable population with limited economic resources, we found that the most frequent opportunistic infections in patients with HIV infection were cerebral toxoplasmosis, meningeal cryptoccocosis, neurosyphilis, and meningeal tuberculosis. In this group of patients, in-hospital mortality amounted to 25.3%. We have found no other studies describing a higher mortality rate in patients with meningeal cryptococcosis infec-

<table>
<thead>
<tr>
<th>Diagnosis, n (%)</th>
<th>Fever</th>
<th>Headache</th>
<th>Altered level of consciousness</th>
<th>Meningeal signs</th>
<th>Epileptic seizure</th>
<th>Cerebral toxoplasmosis</th>
<th>Meningeal cryptoccocosis</th>
<th>Meningeal tuberculosis</th>
<th>Neurosyphilis</th>
<th>Other infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs and symptoms at admission, n (%)</td>
<td>30 (40)</td>
<td>48 (64)</td>
<td>18 (24)</td>
<td>15 (20)</td>
<td>18 (24)</td>
<td>28 (37.3)</td>
<td>15 (20)</td>
<td>7 (9.3%)</td>
<td>15 (20)</td>
<td>10 (13.3)</td>
</tr>
<tr>
<td>Mean time since diagnosis of HIV infection, months (SD)</td>
<td>28.4 (17.3)</td>
<td>19 (25.3)</td>
<td>19 (25.3)</td>
<td></td>
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<tr>
<td>Mean time between symptom onset and consultation, days (SD)</td>
<td>20.5 (48.9)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean hospital stay, days (SD)</td>
<td>28.4 (17.3)</td>
<td>19 (25.3)</td>
<td>19 (25.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU admission, n (%)</td>
<td>19 (25.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Death, n (%)</td>
<td>19 (25.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The variables associated with in-hospital mortality were fever at admission (P = .02), diagnosis of meningeal cryptoccocosis (P = .02), and admission to the ICU (P = .004). We also observed that mortality risk increased by 1.28 times for every 1000 neutrophils in the blood count (P = .015) and by 1.14 times for every increment of mg/dL in blood urea nitrogen (BUN) (P = .003) (Table 3).

Additionally, we observed a decrease in mortality risk associated with each 10 cell/μL increment in the CD4 T lymphocyte count (P = .02), with CSF/blood glucose ratios above 0.5 (P = .07), and with BMI within normal ranges (18–25) (P = .03) (Table 3).

### Discussion

In a vulnerable population with limited economic resources, we found that the most frequent opportunistic infections in patients with HIV infection were cerebral toxoplasmosis, meningeal cryptoccocosis, neurosyphilis, and meningeal tuberculosis. In this group of patients, in-hospital mortality amounted to 25.3%. We have found no other studies describing a higher mortality rate in patients with meningeal cryptococcosis infections. Published studies have focused on the mortality associated with certain opportunistic neurological infections, such as cryptoccocosis and meningeal tuberculosis, and describe mortality rates ranging from 13% to 44%.8,12,13

In our study, the variables associated with higher mortality rates were fever, meningeal cryptoccocosis infection, ICU admission, increased neutrophil count, and increased BUN. The variables associated with a lower risk of mortality were CSF/blood glucose ratio > 0.5, high CD4 T lymphocyte counts, and normal body mass index.

Fever in the context of immunosuppression or neutropenia has been described as a manifestation of severe infection, and increases the mortality risk by up to 50% if the infection is not adequately treated within the first 48 h.14 Presence of fever is reported to be correlated with a lower mortality rate in patients with fever at admission (P = .02), diagnosis of meningeal cryptoccocosis (P = .02), and admission to the ICU (P = .004). We also observed that mortality risk increased by 1.28 times for every 1000 neutrophils in the blood count (P = .015) and by 1.14 times for every increment of mg/dL in blood urea nitrogen (BUN) (P = .003) (Table 3).

Additionally, we observed a decrease in mortality risk associated with each 10 cell/μL increment in the CD4 T lymphocyte count (P = .02), with CSF/blood glucose ratios above 0.5 (P = .07), and with BMI within normal ranges (18–25) (P = .03) (Table 3).
Regarding ICU admissions and mortality in patients with HIV infection, variable rates have been described, which have decreased since the implementation of ART; however, they remain high, and vary according to the region studied, fluctuating between 20–30% in Europe and North America, and 37–68% in such countries as Chile, Brazil, Mexico, China, and Australia. This seems to be related to a poorer immunovirological status in patients admitted to the ICU.\(^{22,23}\) This is in line with our results, which showed that admission to the ICU was associated with 5.8 times greater risk of mortality.

With regard to the increase in BUN, altered renal function has been described in the initial stages of HIV infection\(^ {24}\) and in the presence of such opportunistic infections as tuberculosis and histoplasmosis\(^ {25,26}\); however, BUN has not been studied as a factor associated with mortality, and further studies are needed in this regard. Regarding neutrophil counts, neutropenia frequently manifests in HIV infection, due to a range of mechanisms.\(^ {14}\) Its impact has been mainly studied in cryptococcosis, and neutrophils are considered part of the host immune response, playing a regulatory role in the balance of Th1/Th2 responses. Its effect on the outcomes of the infection may be beneficial or detrimental depending on the type of pathogen involved.\(^ {27}\) In the specific case of cryptococcosis, studies with animal models report that an increase in neutrophil count is associated with a more severe Th1 response that may lead to greater tissue damage and poorer clinical outcomes. On the other hand, in the context of neutropenia, a greater Th2 response is generated, with increased production of IL-4 and IL-10, which may help reduce the tissue damage as a result of the

Table 2 Paraclinical symptoms.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n (%)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral load, copies/mL</td>
<td>4,794,891 (1495526)</td>
<td></td>
</tr>
<tr>
<td>CD4 T lymphocyte count, cells/mm(^3) (n = 69)</td>
<td>102.6 (123.4)</td>
<td></td>
</tr>
<tr>
<td>Blood chemistry study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.03 (1.62)</td>
<td></td>
</tr>
<tr>
<td>BUN, mg/dL</td>
<td>14.01 (6.8)</td>
<td></td>
</tr>
<tr>
<td>Sodium, mmol/L</td>
<td>137.3 (5.02)</td>
<td></td>
</tr>
<tr>
<td>Lumbar puncture</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opening pressure, cm H(_2)O</td>
<td>58 (77.3)</td>
<td></td>
</tr>
<tr>
<td>(normal range: 6–25 cm H(_2)O)</td>
<td>41 (71.9)</td>
<td></td>
</tr>
<tr>
<td>&gt; 25</td>
<td>57 (76)</td>
<td></td>
</tr>
<tr>
<td>CSF glucose level, mg/dL</td>
<td>26 (44.8)</td>
<td></td>
</tr>
<tr>
<td>&gt; 45</td>
<td>32 (55.2)</td>
<td></td>
</tr>
<tr>
<td>CSF protein level</td>
<td>21 (36.2)</td>
<td></td>
</tr>
<tr>
<td>&gt; 45</td>
<td>37 (63.8)</td>
<td></td>
</tr>
<tr>
<td>CSF/blood glucose ratio</td>
<td>34 (61.3)</td>
<td></td>
</tr>
<tr>
<td>&lt; 0.5</td>
<td>21 (38.2)</td>
<td></td>
</tr>
<tr>
<td>Leukocytes, cells/mm(^3)</td>
<td>36 (62.1)</td>
<td></td>
</tr>
<tr>
<td>&gt; 5</td>
<td>22 (37.9)</td>
<td></td>
</tr>
<tr>
<td>Complete blood count</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukocytes, cells/mm(^3)</td>
<td>12 (16)</td>
<td></td>
</tr>
<tr>
<td>4000–11,000</td>
<td>54 (72)</td>
<td></td>
</tr>
<tr>
<td>&gt; 11,000</td>
<td>9 (12)</td>
<td></td>
</tr>
<tr>
<td>Lymphocytes, cells/mm(^3)</td>
<td>12 (16)</td>
<td></td>
</tr>
<tr>
<td>&lt; 800</td>
<td>52 (69.3)</td>
<td></td>
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<tr>
<td>800–5000</td>
<td>11 (14.7)</td>
<td></td>
</tr>
<tr>
<td>&gt; 5000</td>
<td>11 (14.7)</td>
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<tr>
<td>Neutrophils, cells/mm(^3)</td>
<td>11 (14.7)</td>
<td></td>
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<tr>
<td>&gt; 1500</td>
<td>57 (76)</td>
<td></td>
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<tr>
<td>1500–8000</td>
<td>7 (9.3)</td>
<td></td>
</tr>
<tr>
<td>&gt; 8000</td>
<td>9 (12)</td>
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<tr>
<td>Platelets</td>
<td>59 (78.7)</td>
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<tr>
<td>&lt; 150,000</td>
<td>7 (9.3)</td>
<td></td>
</tr>
<tr>
<td>150,000–400,000</td>
<td>102.6 (123.4)</td>
<td></td>
</tr>
<tr>
<td>&gt; 400,000</td>
<td>54 (72)</td>
<td></td>
</tr>
<tr>
<td>CRP</td>
<td>12 (16)</td>
<td></td>
</tr>
<tr>
<td>&gt; 0.5</td>
<td>54 (72)</td>
<td></td>
</tr>
<tr>
<td>Simple head CT scan</td>
<td>44 (60.3)</td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

and 37–68% in such countries as Chile, Brazil, Mexico, China, and Australia. This seems to be related to a poorer immunovirological status in patients admitted to the ICU.\(^ {22,23}\) This is in line with our results, which showed that admission to the ICU was associated with 5.8 times greater risk of mortality.

Table 3 Variables associated with decreased and increased mortality risk in patients with HIV-associated opportunistic neurological infection.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (18–25)</td>
<td>0.24</td>
<td>0.067–0.87</td>
<td>0.03</td>
</tr>
<tr>
<td>CD4 T lymphocyte count (×10)</td>
<td>0.85</td>
<td>0.74–0.97</td>
<td>0.020</td>
</tr>
<tr>
<td>CSF/blood glucose ratio (&gt; 0.5)</td>
<td>0.07</td>
<td>0.001–0.58</td>
<td>0.004</td>
</tr>
<tr>
<td>Increased mortality risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningeal cryptococcosis</td>
<td>5.25</td>
<td>1.29–21.35</td>
<td>0.02</td>
</tr>
<tr>
<td>Fever</td>
<td>3.61</td>
<td>1.07–12.63</td>
<td>0.02</td>
</tr>
<tr>
<td>ICU admission (yes/no)</td>
<td>5.8</td>
<td>1.57–21.27</td>
<td>0.004</td>
</tr>
<tr>
<td>Neutrophils (×1000)</td>
<td>1.28</td>
<td>1.04–1.56</td>
<td>0.015</td>
</tr>
<tr>
<td>Blood urea nitrogen</td>
<td>1.14</td>
<td>1.04–1.26</td>
<td>0.003</td>
</tr>
</tbody>
</table>
inflammatory process; together with a decreased Th1 response, this would explain why neutropenic animal models present better survival. 28 This is consistent with our own results and may explain why the increase in the total neutrophil count was associated with an increased mortality risk.

With respect to CD4 T lymphocyte count, higher levels have been associated with a lower mortality rate, especially with counts higher than 200 cells/mm³. 29 This is in line with our results, which showed a decrease in mortality risk with every increment of 10 cells/mm³. Viral load was also identified as a direct marker of HIV infection, with an increase of 10⁴ copies/mL being associated with 1.02 times greater mortality risk.

Low CSF glucose levels have been described as a predictor of mortality in the first year after neurological infection in HIV-positive patients. 30 This is consistent with our results, which showed lower mortality risk in patients with a normal CSF/blood glucose ratio (> 0.5). Furthermore, an association between low body weight and mortality has been described in patients with HIV infection, and it is reported that mortality risk decreases as body weight increases. 31 In our study, we observed that a normal BMI was associated with lower mortality rate.

In our population, a high percentage of patients (68.2%) with a known diagnosis of HIV infection were not receiving ART. Adherence to ART is an essential factor in predicting the clinical outcomes and mortality rate associated with HIV infection. 32, 33 Some studies have found that lack of adherence to ART is a risk factor for viral changes (transient increases of HIV RNA in plasma), virological failure, drug resistance, and increased mortality. 34 Additionally, since the 1990s, ART programmes have been established in Latin America, the Caribbean, South-East Asia, and Sub-Saharan Africa; however, treatment access still represents a challenge, especially in developing countries. 34, 35 In Latin America and the Caribbean, only 42% of individuals are estimated to receive treatment. 36 Despite this, we did not find a statistically significant association between treatment adherence and mortality; however, our methodology was not designed to predict causal associations, and more specific studies are therefore needed to establish more precise associations in our population.

Limitations

The main limitations of our study are related to the retrospective data collection. The lack of data is clear for some variables. Additionally, our sample was collected from the database of a single hospital, with patients being selected by convenience sampling, which may have led to a selection bias. The specific conditions of the population attended at our hospital are not representative of the general population; therefore, the results are only applicable to similar populations to that described. There may be an information bias related to the patient interview performed at admission as, despite being conducted by specialist physicians and residents with sufficient training, the interview is not standardised, and questions regarding symptoms may not have been the same for all the reported symptoms. Lastly, there is a possible Neyman bias regarding patients with neurosyphilis, which is relatively frequently diagnosed after active search in patients with HIV infection and no neurological symptoms but with serological diagnosis of late latent syphilis.

Conclusions

In our public hospital, which attends a population with limited socioeconomic resources, toxoplasmosis is the most frequently diagnosed CNS opportunistic infection in patients with HIV infection. However, meningal cryptococcosis is the infection associated with the greatest increase in mortality risk. Approximately one in every 4 patients dies, and mortality is higher in those presenting fever at admission, requiring ICU admission, with higher total blood neutrophil count, and with increased BUN concentration. On the contrary, mortality is lower in those with normal BMI, with higher CD4 T lymphocyte count, and without low CSF glucose level. These findings help us to define the parameters to be closely monitored in patients with HIV infection and opportunistic neurological infections. The methodology of this study does not allow us to establish causal associations, but our results may be useful in the design of prevention policies to decrease mortality among these patients. Further prospective studies are needed to confirm these findings.

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None

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neurop.2023.100127.

References


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