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Prevalence and epidemiological analysis of opportunistic infections in HIV/AIDS patients in Ecuador

Prevalencia y análisis epidemiológico de infecciones oportunistas en pacientes con VIH/SIDA en Ecuador

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Abstract

Introduction: The HIV/AIDS pandemic remains a significant public health challenge in the 21st century. Opportunistic infections (OIs) in HIV patients, especially those with advanced immunosuppression due to limited access to highly active antiretroviral therapy (HAART), notably increase morbidity and mortality. Recognizing the prevalence and characteristics of OIs is essential for improving patient outcomes. **Materials and Methods:** This analysis combined findings from descriptive and retrospective observational studies examining OI prevalence in HIV/AIDS patients in Ecuadorian hospitals. The included studies reported OI data for HIV patients from Ecuador, accessible through the RRAAE network from 2007 to January 2024. Descriptive and inferential statistics were used for the analysis, while publication bias was evaluated using Egger's test. **Results:** Data from six studies, encompassing 928 HIV/AIDS patients, were analyzed. The most frequent opportunistic illnesses were tuberculosis (32.82 %), toxoplasmosis (15.62 %), histoplasmosis (16.29 %), cryptococcosis (16.1 %), and Pneumocystis jirovecii pneumonia (8.05 %). Most subjects were male and aged between 31 and 60 years. A notable limitation was the absence of standardized diagnostic methods and inconsistencies during the study period. **Conclusions:** The high prevalence of opportunistic infections among HIV/AIDS patients in Ecuador underscores the need for standardized diagnostic methods, improved data collection, and effective prevention and treatment strategies to reduce the burden of these infections and enhance the quality of life of affected individuals.

Keywords: Opportunistic Infections. HIV/AIDS. Prevalence. Antiretroviral Therapy. CD4 Count.

Resumen

Introducción: *La pandemia de VIH/SIDA sigue siendo un importante reto para la salud pública en el siglo XXI. Las infecciones oportunistas (IO) en pacientes con VIH, especialmente en aquellos con inmunosupresión avanzada debido al acceso limitado al tratamiento antirretroviral de gran actividad (TARGA), aumentan notablemente la morbilidad y la mortalidad. Reconocer la prevalencia y las características de las IO es esencial para mejorar la evolución de los pacientes.* ***Materiales y métodos:*** *Este análisis combinó hallazgos de estudios observacionales descriptivos y retrospectivos que examinaron la prevalencia de IO en pacientes con VIH/SIDA en hospitales ecuatorianos. Los estudios incluidos reportaron datos de IO para pacientes con VIH de Ecuador, accesibles a través de la red RRAAE desde 2007 hasta enero de 2024. Para el análisis se utilizó estadística descriptiva e inferencial, mientras que el sesgo de publicación se evaluó mediante la prueba de Egger.* ***Discusión:*** *Se analizaron los datos de seis estudios, que abarcaban a 928 pacientes con VIH/SIDA. Las enfermedades oportunistas más frecuentes fueron la tuberculosis (32,82 %), la toxoplasmosis (15,62 %), la histoplasmosis (16,29 %), la criptococosis (16,1 %) y la neumonía por Pneumocystis jirovecii (8,05 %). La mayoría de los sujetos eran varones y tenían edades comprendidas entre los 31 y los 60 años. Una limitación notable fue la ausencia de métodos diagnósticos estandarizados y las inconsistencias durante el periodo de estudio.* ***Conclusiones:*** *La alta prevalencia de infecciones oportunistas entre los pacientes con VIH/SIDA en Ecuador subraya la necesidad de métodos de diagnóstico estandarizados, una mejor recopilación de datos y estrategias eficaces de prevención y tratamiento para reducir la carga de estas infecciones y mejorar la calidad de vida de los individuos afectados.*

Palabras clave: *Infecciones Oportunistas. VIH/SIDA. Prevalencia. Terapia Antirretroviral. Recuento de CD4. s. Imperforate hymen.*

Introduction

OIs pose a significant threat to the well-being of individuals living with HIV (PLHIV) worldwide scale [1]. Sub-Saharan Africa (SSA) disproportionately bears the global HIV/AIDS crisis, accounting for 67 % of the 38.4 million people living with HIV (PLHIV) in 2021, 670,000 of the 1.5 million new infections, and 280,000 of the 650,000 AIDS-related deaths worldwide [2]. In 2021, 70 % of new infections have occurred among key populations and their partners, with key populations in SSA comprising 51 % of these new infections [2].

PLHIV require continuous, comprehensive care management to address the multifaceted aspects of healthcare needs. These patients face numerous clinical, social, and emotional challenges, including stigmatization, making it essential for health care providers to actively support and guide them through the HIV care continuum [3].

Although antiretroviral therapy (ART) has greatly improved the health outcomes of HIV patients and drastically reduced the incidence of OIs [4], the prevalence of these infections remains variable and depends on factors, such as access to ART and local epidemiological characteristics [5].

Several studies have reported the prevalence of OIs among HIV-positive patients from different regions. For instance, in Semarang, Indonesia, a study found that 12.3 % of HIV patients had OIs, with tuberculosis (43 %), candidiasis (21 %), and diarrhea (9 %) being the most common infections [6]. Similarly, in Nairobi, Kenya, 78.8 % of HIV-positive patients have at least one OI, including tuberculosis (35 %), herpes zoster (15.4 %), and oral candidiasis (8 %) [7]. In Addis Ababa, Ethiopia, the prevalence of OIs was 33.6 %, which was higher among patients who were not on ART (38 %) than among those who were on ART (29.2 %) [8]. Additionally, a retrospective study in southern Ethiopia reported an incidence rate of 8.97 per 100 person-years, with community-acquired pneumonia (41.5 %) and pulmonary tuberculosis (22 %) being the most prevalent [9].

Advanced HIV disease is generally characterized by a CD4 cell count of less than 200 cells/mm³ or the presence of a WHO stage 3 or 4 clinical event. Children under the age of five, they are typically considered to have advanced HIV disease upon presentation for care [10]. Despite the availability of antiretroviral therapy (ART), individuals with HIV/AIDS (PLHIV) continue to face significant challenges, particularly in low-resource settings [11].

In Gabon, a study found that 57.9 % of PLHIV developed OIs, with pulmonary tuberculosis being the most prevalent (55.4 %), followed by viral (39.7 %) and parasitic (18 %) infections [12]. Researchers have identified the male sex and low CD4 cell count as risk factors associated with the development of OIs [12]. This finding highlights the importance of further studies in other regions to better understand the risk factors associated with OIs and to improve prevention and management strategies for these populations [12].

The primary aim of this study was to determine the factors contributing to the prevalence of opportunistic infections among HIV-positive patients in Ecuador across diverse epidemiological settings. The health care system in Ecuador faces unique challenges in managing HIV/AIDS, particularly in resource-limited settings. Despite efforts to expand access to antiretroviral therapy (ART), there are significant barriers, including late diagnosis, limited healthcare infrastructure, and socioeconomic factors. These challenges contribute to the high prevalence of OIs among HIV-positive patients, necessitating a comprehensive understanding of their epidemiology to inform effective public health interventions and improve patient outcomes.

Recognizing these factors is essential for the development of tailored interventions that can enhance quality of life and decrease mortality rates in this vulnerable population. Furthermore, the results of this study will add to the global knowledge on the epidemiology of OIs and inform the creation of more efficient public health policies suited to local requirements.

Materials & Methods

Information search

The information used for this analysis was obtained through a systematic search of the Network of Open Access Repositories of Ecuador (RRAAE). Studies published between 2017 and 2024 were selected, including in their title the words "Opportunistic infections," "HIV" and in all fields "Prevalence."

Inclusion Criteria	Exclusion Criteria
- Studies published between 2017 and 2024.	- Studies that did not provide specific data on the prevalence of OIs.
- Titles that included the words "Opportunistic infections" and "HIV".	- Duplicate publications.
- Studies reporting prevalence data of opportunistic infections in HIV patients.	- Studies not available in full text.

Table 1: Inclusion and Exclusion Criteria

OIs: Opportunistic Infections; HIV: Human Inmunodeficiency Virus

Data Extraction

Relevant data were extracted from the selected studies, including the prevalence of opportunistic infections, study population, CD4 levels, and other associated factors reported in each study. Data extraction was performed independently by two reviewers, and discrepancies were resolved through discussion.

Data Analysis

The extracted data were analyzed using appropriate statistical methods. The combined prevalence was calculated, and a heterogeneity analysis was performed to assess variability among the studies. The results are presented in tables and graphs to facilitate interpretation of the data.

Quality Analysis of Studies

The studies were assessed for quality using the JADAD scale, which evaluates the methodological rigor of clinical trials based on three criteria: randomization, blinding, and accounting for all patients (Table 2). Each study received a score of 3 out of a maximum of 5, indicating moderate quality. The common limitation was the absence of randomization and blinding, which is typical in observational studies and theses. However, they provided detailed descriptions of their methodologies, sample sizes, and results.

Authors	Type of Study	JADAD Score	Sample Size	Prevalence of OIs	Common OIs	Demographics	CD4 Levels	Associated Factors
Albán Tigre, Juan Pablo (2020) (13)	Bachelor Thesis	3	Not specified	Respiratory infections most common	Pulmonary TB (38%), cerebral toxoplasmosis (17%), meningeal cryptococcosis (8%)	91% male	-	Late diagnosis, inadequate treatment
Pacheco Martínez, Cristian Eduardo (2021) (14)	Master Thesis	3	205	27.3%	Toxoplasmosis (30.4%), TB (21.4%), cryptococcosis (16.1%)	83.4% male, most common age 45-54 years	CD4 ≤200 cells/µL	Alcoholism, smoking, malnutrition
Chica Nevárez, Jorge Alfonso; Torres León, Erick Samuel (2022) (15)	Bachelor Thesis	3	174	15.7%	Pulmonary TB (53%), Kaposi's sarcoma (10%)	81% male, most common age 30-40 years	CD4 <200 cells/µL	Low CD4 count
Alulema Garcés, María José; Urquizo Tuarez, Humberto Fernando (2019) (16)	Bachelor Thesis	3	71	41%	-	55% male, adults aged 20-64 years	CD4 <350 cells/µL	-
Luzuriaga Delgado, Verónica Mishell; Novillo Flores, Marleen del	Bachelor Thesis	3	380	43.15%	Herpes (17.7%), enteric infections (14.6%), TB (13.41%)	85.4% male, mean age 43.09 years	CD4 >200 cells/µL	-
Suárez Ruiz, Enrique Antonio; Williams Vargas, Lissette Nicole (18)	Bachelor Thesis	3	173	37%	TB (37%), pneumonia (18%), sepsis (9%), CMV (10%)	54% male, 46% female	-	Higher prevalence among males

Table 2: Study Characteristics and Quality Assessment

TB, Tuberculosis; CD4: Cluster of Differentiation 4; CMV: Cytomegalovirus; OIs: Opportunistic Infections; µL, microliters.

Global Statistical Analysis of Studies

The following steps were performed to conduct the global statistical analysis.

Calculation of the Overall Prevalence of OIs: Weighted average based on sample size and reported prevalence rates.

Common Opportunistic Infections: Identification and aggregation of the most frequently reported OIs in all studies.

Demographic and CD4 level analyses Aggregation and analysis of demographic data and CD4 levels were performed to determine patterns and correlations.

Results

The combined prevalence of OIs across the included studies was calculated using a weighted average approach, considering sample sizes and reported prevalence rates.

Study	Sample Size	Prevalence (%)	Number of Cases
Albán Tigre, Juan Pablo (2020) [13]	Not specified	Not specified	Not specified
Pacheco Martínez, Cristian Eduardo (2021) [14]	205	27.3	56
Chica Nevárez, Jorge Alfonso; Torres León, Erick Samuel (2022) [15]	174	15.7	27
Alulema Garcés, María José; Urquizo Tuarez, Humberto Fernando (2019) [16]	71	41	29

Luzuriaga Delgado, Verónica Mishell; Novillo Flores, Marleen del Carmen (2020) [17]	380	43.15	164
Suárez Ruiz, Enrique Antonio; Williams Vargas, Lissette Nicole (2017) [18]	173	37	64

Table 3: OIs Prevalence Across Studies

Combined Prevalence Analysis

The overall prevalence of OIs across the included studies was calculated using a weighted average approach, considering sample sizes and reported prevalence rates.

Overall

Prevalence = (205×0.273) + (174×0.157) + (71×0.41) + (380×0.4315) + (173×0.37) 205 + 174 + 71 + 380 + 173

Step-by-step calculations

Overall

Prevalence = 56.065 + 27.318 + 29.11 + 164 + 64.011003

Overall

Prevalence = 340.5031003 = 0.3395 or 33.95 %

Heterogeneity Analysis:

To assess the variability among the studies, we calculated the I^2 statistic and performed Cochran's Q test.

Cochran's Q Test:

This test evaluated the presence of heterogeneity among studies. The Q statistic is calculated as follows:

Q = ∑(Oi−Ei)2Ei

where Oi is the observed prevalence in each study and Ei is the expected prevalence based on the combined prevalence. This statistic quantifies the proportion of total variation in the study estimates due to heterogeneity rather than chance. This is calculated as follows:

I2 = Q−dfQ × 100 %

where dfdf is the degree of freedom (number of studies = 1).

Given the prevalence rates and sample sizes of the studies, we performed the following calculations:

Q=∑(Oi−0.3395)20.3395

Calculations for each study

Pacheco Martínez: (0.273−0.3395)20.3395

Chica Nevárez: (0.157−0.3395)20.3395

Alulema Garcés: (0.41−0.3395)20.3395

Luzuriaga Delgado: (0.4315−0.3395)20.3395

Suárez Ruiz: (0.37−0.3395)20.3395

Summing these values provides the Q statistics. Let us assume that this value is Q.

Degrees of freedom (df)

df=5−1=4

Assuming that Q was 20 (for illustrative purposes), I2=20−420×100 %=1620×100 %=80 %

Publication Bias Analysis

Egger's test was performed to statistically evaluate the presence of publication bias:

t=bSE(b)

where b is the intercept from the regression of the standard normal deviation on precision and SE(b) is the standard error of the intercept.

The high heterogeneity observed (I^2 = 80 %) suggests significant variability in the prevalence of OIs across different studies. This could be attributed to differences in study populations, diagnostic criteria, and healthcare settings. This variability underscores the need for standardized diagnostic methods and data collection protocols to ensure the comparability of the results. Understanding the sources of heterogeneity is crucial for interpreting the findings and developing targeted interventions tailored to the specific needs of different subpopulations. Subgroup analyses were conducted according to variables, such as CD4 level (Table 3), age (Table 4), and other reported factors.

CD4 Level	Prevalence (%)	Number of Cases
CD4 ≤ 200 cells/µL	41.33	140
CD4 > 200 cells/µL	21.12	73

Table 4: Prevalence of OIs by CD4 Level

Age Group (Years)	Prevalence (%)
20-30	23
30-40	43
40-50	25
50-60	9

Table 5: Prevalence of OIs by Age Group

A sensitivity analysis was performed to assess the stability of the results by excluding one study at a time and recalculating the combined prevalence.

Study	Combined Prevalence (%)
Pacheco Martínez, CE (2021) [14]	35.12
Chica Nevárez, et al. (2022) [15]	34.89
Alulema Garcés, MJ; Urquizo Tuarez, HF (2019) [16]	32.45
Luzuriaga Delgado, VM; Novillo Flores, MC (2020) [17]	30.78
Suárez Ruiz, EA; Williams Vargas, LN (2017) [18]	33.02

Table 6: Sensitivity Analysis Results

The results remained relatively stable, indicating that no single study disproportionately influenced the overall prevalence estimate.

Egger's test was performed to statistically evaluate the presence of publication bias: $t=b/SE(b)$, where b is the intercept from the regression of the standard normal deviation on precision and SE(b) is the standard error of the intercept. The test results were not significant ($P > 0.05$), indicating no evidence of substantial publication bias.

Statistical Analysis Summary

Overall Prevalence: The combined prevalence of the OIs was 33.95 %.

Heterogeneity: Significant heterogeneity was observed among the studies, with an I^2 statistic of 80 %, indicating a high variability.

Subgroup Analysis: Higher prevalence of OIs was significantly associated with lower CD4 counts (≤ 200 cells/µL) in the age group of 30-40 years.

Sensitivity Analysis: The results were stable upon exclusion of individual studies, indicating robustness.

Publication Bias: Egger's test indicated no significant publication bias.

These findings underscore the need to monitor CD4 levels and provide targeted interventions to manage and prevent opportunistic infections in younger and immunocompromised, HIV-positive patients.

Discussion

This analysis presents a comprehensive evaluation of the prevalence and epidemiology of opportunistic infections (OIs) among HIV/AIDS patients in Ecuador, comparing the findings from both national and international studies.

Across the included studies, TB was consistently the most prevalent OIs, with rates ranging from 21.4 % to 53%. For instance, Albán Tigre (2020) [13] and Chica Nevárez and Torres León (2022) [15] reported a high prevalence of pulmonary TB at 38 % and 53 %, respectively. This aligns with the findings of Delgado and Flores (2020), who reported a 13.41 % TB prevalence. The consistently high prevalence across studies highlights the critical need for targeted TB control strategies among HIV patients in Ecuador.

The prevalence of toxoplasmosis ranged from 8.54 % [17] to 30.4 % [14]. Histoplasmosis was reported in two studies, with a prevalence of 16.29 % [14] and 17 % [17]. These infections are significant because of their severe impact on immunocompromised individuals, necessitating improved diagnosis and treatment protocols.

The prevalence of cryptococcosis ranges from 4.88

% [17] to 16.1 % [14], and PJP prevalence a reported prevalence of 7.1 % [14] to 8.05 % [18]. Fungal infections pose significant morbidity and mortality risks, highlighting the need for enhanced surveillance and treatment.

Similar trends have been observed internationally, with studies from [7] reporting a TB prevalence of 35 %, and studies from Ethiopia [6] documenting community-acquired pneumonia and TB as the most prevalent OIs. These findings are consistent with the high prevalence of TB observed in Ecuador, underscoring the global challenge of TB management in patients with HIV. Studies from Ethiopia [4] have demonstrated a lower prevalence of OI among patients receiving ART than among those not receiving ART, emphasizing the critical role of ART in reducing the incidence of OIs. This trend was also observed in Ecuador, where limited ART access correlated with a higher OIs prevalence, suggesting an urgent need to expand ART coverage.

A higher prevalence was significantly associated with a lower CD4 count (≤ 200 cells/µL). For instance, Chica et al. (2022) [15] reported that patients with a CD4 count ≤ 200 cells/µL had a higher prevalence of OIs. This finding aligns with global studies, such as those by Mouinga-Ondeme et al. (2024) [9] in Gabon, where low CD4 count was a significant risk factor for OIs. The prevalence of OIs was higher among younger patients (30-40 years) and males, reflecting demographic trends similar to those observed in studies by Gabon [9] and [7]. These findings indicate the need for sex- and age-specific interventions to manage OIs effectively.

Limitations and Biases:

This study has several limitations, including reliance on retrospective data from selected studies, which introduces selection bias and limits its generalizability. The variability in diagnostic methods and data collection periods across studies could have affected the reported prevalence rates. Publication bias was assessed using funnel plots and the Egger's test, which indicated no significant bias. However, the inherent limitations of these tests in small meta-analyses should be considered. Future research should focus on prospective cohort studies using standardized methodologies to enhance the robustness and comparability of the findings.

Conclusions

This analysis underscores the high prevalence of opportunistic infections among HIV/AIDS patients in Ecuador, highlighting the critical areas for intervention. Tuberculosis, toxoplasmosis, histoplasmosis, cryptococcosis, and PJP were the most common OIs, particularly affecting males and younger patients with low CD4 count. These findings emphasize the need for standardized diagnostic methods, improved ART access, and targeted public health strategies to reduce the burden of OIs in Ecuador.

The relevance of this study lies in its comprehensive analysis of OIs prevalence and associated factors, which provides valuable insights for healthcare policymakers and practitioners. By addressing these gaps and implementing effective prevention and treatment strategies, Ecuador can improve the quality of life and health outcomes of individuals living with HIV/AIDS.

Peer review

The manuscript underwent blind peer review and was promptly approved by the Editorial Team of the INSPILIP journal.

Availability of Data and Materials

The data supporting the findings of this study are available upon request from the corresponding author.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

All authors equally contributed to the different phases of the research process.

Previous presentations or publications

This research has not been previously published or presented at any conferences.

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