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Occurrence of Severe Opportunistic Infections in Children Living with HIV Under Regular Follow-Up in Lubumbashi: Associated Factors and Clinical Implications

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Abstract

Introduction: Despite expanded access to antiretroviral therapy (ART), opportunistic infections (OIs) remain a leading cause of morbidity and mortality among children living with HIV in sub-Saharan Africa. In the Democratic Republic of Congo, the persistence of severe OIs in children under regular follow-up suggests the presence of underrecognized risk factors. This study aimed to identify factors associated with the occurrence of severe OIs among HIV-infected children in Lubumbashi.

Methods: We conducted a retrospective, analytical study from January 2020 to December 2024 at the HIV/AIDS Center of Excellence in Lubumbashi. A total of 175 children aged 2 to 14 years were included. Clinical, biological, nutritional, and behavioral data were analyzed using Jamovi software.

Results: Severe OIs were reported in 33.1% of cases. Factors significantly associated with adverse outcomes (death or sequelae) included CD4 count < 500 cells/mm^3, ART adherence < 80%, delayed HIV diagnosis, and missed clinic visits. Conversely, adherence ≥ 95% was associated with a favorable outcome in 92.3% of cases.

Conclusion: Severe OIs remain common among children living with HIV despite regular care. Optimizing early diagnosis, improving ART adherence, and implementing targeted support strategies are essential to reduce HIV-related complications and improve pediatric outcomes in resource-limited settings.

Keywords: Pediatric HIV; Opportunistic Infections; Adherence; Risk Factors; Democratic Republic of Congo

1. Introduction

The human immunodeficiency virus (HIV) remains, despite notable therapeutic progress, one of the leading causes of childhood mortality in sub-Saharan Africa, where nearly 1.7 million children under the age of 15 are living with HIV,

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accounting for more than 85% of the global pediatric burden (UNAIDS, 2023). Among children living with HIV (CLHIV), the progressive immunosuppression induced by the virus creates a favorable environment for the development of opportunistic infections (OIs), which continue to represent the main cause of hospitalization and death, despite the expansion of access to antiretroviral therapy (ART) (WHO, 2022; Peacock-Villada et al., 2014). Delayed ART initiation, poor adherence, the presence of comorbidities such as severe malnutrition, and socioeconomic vulnerability are all factors that worsen the prognosis of these already fragile children (Low et al., 2016; Mwiru et al., 2015).

In the Democratic Republic of Congo (DRC), particularly in Lubumbashi, the implementation of the National Strategic Plan against HIV has led to significant progress in screening and ART initiation among children. However, severe OIs are still observed, including in pediatric patients who receive regular follow-up in referral centers such as the HIV/AIDS Center of Excellence. This persistence suggests the presence of underlying risk factors that remain poorly documented and highlights the need for further research in this area.

Despite regular medical follow-up, some children living with HIV continue to develop severe OIs. This raises questions about the clinical (WHO stage, vaccination status), biological (CD4 count, viral load, hematology), nutritional (acute or chronic malnutrition), and socio-environmental (caregiver's educational level, geographic distance, living conditions) determinants that may influence this vulnerability. In the absence of recent, robust local data, it remains difficult to establish a risk profile that would allow clinicians to anticipate these complications.

Hence, our research question

What are the factors associated with the occurrence of severe opportunistic infections among children living with HIV under regular follow-up in Lubumbashi?

2. Methods

2.1. Study design and setting

We conducted a retrospective, analytical, quantitative study at the HIV/AIDS Center of Excellence in Lubumbashi (Haut-Katanga Province, DRC), a referral structure providing comprehensive, free, and multidisciplinary care for children living with HIV. The study covered a five-year period, from January 1, 2020, to December 31, 2024.

2.2. Study population

2.2.1. Inclusion criteria

All children aged 2 to 14 years, regardless of sex, living with HIV and continuously followed at the Center of Excellence for at least 12 months between January 2020 and December 2024 were included. HIV infection was confirmed according to national criteria (rapid tests, PCR, or Western Blot in doubtful cases). Only complete medical records containing essential clinical, biological, and therapeutic data were retained. Children with or without a documented severe OI (tuberculosis, pneumocystosis, cryptococcosis, etc.) were included.

2.2.2. Exclusion criteria

Children were excluded if they

were transferred from other centers without exploitable medical history, had major gaps in their records (CD4, viral load, OI diagnoses), or died from a clearly non-infectious cause unrelated to HIV (trauma, drowning, etc.).

2.2.3. Sampling

An exhaustive sampling was performed. All records meeting the inclusion criteria were systematically retained to maximize statistical power and minimize selection bias.

2.3. Variables

2.3.1. Dependent variable

Occurrence of a severe opportunistic infection during follow-up (binary variable: yes/no), defined by hospitalization, an acute life-threatening complication, or the need for intensive treatment.

2.3.2. Independent variables

- Sociodemographic: age, sex, orphan status, caregiver's education level, distance from home to the center.
- Clinical: WHO stage at inclusion, acute malnutrition (weight-for-height z-score < -2), associated comorbidities, frequency of consultations.
- Biological: absolute and percentage CD4 count, viral load (copies/mL), hemoglobin level.

Therapeutic and behavioral: delay between HIV diagnosis and ART initiation, ART regimen, adherence (assessed through appointment keeping, treatment regularity, monthly dispensing), access to psychosocial support (social worker, support group, mentoring).

2.4. Data collection and analysis

Data were extracted using a standardized collection form designed in Excel, based on WHO and National AIDS Program recommendations. After double entry and manual validation, data were imported into Jamovi software (version 2.x) for statistical analysis. This software was chosen for its compatibility with R, transparency, and robustness.

2.5. Ethical considerations

The study was approved by the Ethics Committee of the HIV/AIDS Center of Excellence. All data were anonymized before analysis, in accordance with the principles of the Declaration of Helsinki.

3. Results

A total of 175 children living with HIV were included in the analysis. The mean age at the time of diagnosis was 7.8 ± 3.5 years, reflecting an overall delay in pediatric HIV screening. Sex distribution was balanced, with a slight male predominance (52.6%). Immunologically, the median baseline CD4 count was 460 cells/mm^3 [IQR: 300–650], indicating moderate to severe immunosuppression in a considerable proportion of cases. Regarding baseline viral load, the median was 10,500 copies/mL [IQR: 3,200–35,000], demonstrating active viral replication at inclusion. Mean adherence to ART was estimated at 89.6% ± 12.3, which is generally acceptable but showed notable heterogeneity, suggesting that some patients had suboptimal adherence (Table I, appendix).

Among the included children, 33.1% (n = 58) required hospitalization for an opportunistic infection. The mean number of missed visits per patient was 1.6 ± 1.2, suggesting partially compromised adherence in some cases. The outcome of OIs was generally favorable in 69.7% of cases (n = 122). However, there were 18 deaths (10.3%) directly attributable to an OI, as well as 15 cases (8.6%) with post-infectious sequelae. Notably, 11.4% of records lacked documentation on OI outcome, highlighting a potential limitation in data completeness (Table II, appendix).

A strong association was observed between the level of ART adherence and the outcome of OIs. Among children with adherence ≥ 95%, 92.3% had a favorable outcome, compared to 65.7% for those with adherence between 80% and 94%, and only 41.2% when adherence was below 80%. Conversely, mortality and post-infectious sequelae increased significantly with decreasing adherence. The death rate rose from 3.8% among highly adherent children to 35.3% in the least adherent group, while the frequency of sequelae increased from 3.9% to 23.5%. These findings confirm the central role of treatment adherence in determining prognosis for children living with HIV, particularly in preventing severe OIs, and highlight the urgent need to strengthen adherence support interventions, especially for patients at higher risk of treatment interruption (Table III, appendix).

4. Discussion

4.1. Delayed diagnosis of pediatric HIV

The mean age at HIV diagnosis in our cohort (7.8 ± 3.5 years, Table I) highlights a persistently delayed diagnosis among children living with HIV in Lubumbashi. This delay is concerning because it postpones the initiation of antiretroviral therapy (ART) and exposes children to increased morbidity. This trend has already been documented in sub-Saharan Africa, where more than half of children are diagnosed after the age of five (Mahy et al., 2010; Mofenson and Cotton, 2013). Probable causes include family-related stigma, limited access to early virological testing (PCR), and the lack of systematic integration of HIV screening into primary pediatric care (Dube et al., 2018; Slogrove et al., 2020). Strengthening targeted screening in HIV-exposed infants, as recommended by Lawn et al. (2012) and Nachega et al. (2017), is therefore urgently needed.

4.2. Immuno-virological profile and ART initiation

Immuno-virological findings revealed a median baseline CD4 count of 460 cells/mm^3 and a median viral load of 10,500 copies/mL (Table I), reflecting advanced immunosuppression and high viral replication at inclusion. These results suggest delayed ART initiation, which contrasts with current WHO recommendations advocating for immediate ART initiation regardless of CD4 count (WHO, 2021). Several studies have shown that low CD4 counts and high viral loads are independently associated with increased mortality and morbidity (Newell et al., 2009; Patel et al., 2015; Violari et al., 2008).

4.3. Therapeutic adherence and clinical outcomes

The average adherence observed in our cohort (89.6 ± 12.3%, Table I) masks considerable heterogeneity. Data from Table III reveal a strong association between the level of ART adherence and the clinical outcome of opportunistic infections (OIs). Children with adherence ≥ 95% had favorable outcomes in 92.3% of cases, compared to 41.2% for those with adherence < 80%. In parallel, mortality rates increased from 3.8% in highly adherent children to 35.3% in the least adherent, while the frequency of sequelae rose from 3.9% to 23.5%.

These results confirm the central role of adherence in reducing the risk of severe complications, as previously demonstrated (Paterson et al., 2000; Bangsberg et al., 2001). Psychosocial support, patient–provider relationships, and understanding of therapeutic issues are crucial determinants of adherence (Kahana et al., 2013; Vreeman et al., 2018). Our findings highlight the urgent need to reinforce adherence-support strategies, particularly among patients at high risk of treatment interruption.

4.4. Persistent frequency of severe opportunistic infections and outcomes

Approximately one-third of children (33.1%, Table II) experienced an OI requiring hospitalization, highlighting the continued high burden of these conditions despite regular medical follow-up. Mortality (10.3%) and post-infectious sequelae (8.6%) remain significant (Table II), although lower than those reported in earlier cohorts (Walker et al., 2007). These results underscore the importance of preventive strategies—including early ART initiation, cotrimoxazole prophylaxis, vaccination, and nutritional support—which remain insufficiently implemented in many settings (Penazzato et al., 2015).

The mean number of missed visits (1.6 ± 1.2, Table II) indicates moderate but non-negligible disruptions in continuity of care. It is well established that even short ART interruptions can lead to viral rebound and foster the emergence of resistance (El-Khatib et al., 2011). Structural factors such as geographic distance, economic hardship, and social stigma may contribute to these gaps in care (Cluver et al., 2015). Community-based interventions—such as adherence clubs, SMS reminders, and peer mentoring—have demonstrated effectiveness in similar contexts (Zachariah et al., 2006), yet remain underdeveloped in our environment.

5. Conclusion

This study demonstrated that, despite regular medical follow-up, severe opportunistic infections (OIs) remain frequent among children living with HIV in Lubumbashi, with a prevalence of 33.1% and significant mortality. The factors most strongly associated with these complications were low CD4 count, poor treatment adherence, delayed diagnosis, and missed appointments. Conversely, adherence ≥ 95% to antiretroviral therapy proved to be protective, confirming the central role of adherence in improving pediatric prognosis.

These findings highlight the urgent need to strengthen early screening strategies, therapeutic education, psychosocial support, and community-based interventions to improve adherence and reduce treatment interruptions. They also emphasize the necessity of integrating nutrition, vaccination, and comprehensive management into pediatric HIV programs.

Finally, this study contributes to documenting local challenges and provides guidance for policies and clinical practices in the Democratic Republic of Congo, with the ultimate goal of reducing morbidity and mortality related to opportunistic infections among children living with HIV.

Recommendations

For clinical practice

- Strengthen early HIV screening in children, particularly through systematic integration of virological testing in HIV-exposed infants during the first months of life.
- Improve therapeutic support for children and their families through continuous education on the importance of strict adherence to ART.
- Integrate regular nutritional follow-up into care to limit the impact of malnutrition as an aggravating factor of immunosuppression.
- Implement individualized follow-up systems (SMS reminders, phone calls, home visits) to reduce missed appointments.

For policymakers and health program managers

- Develop and support community-based interventions (adherence clubs, peer mentoring, psychosocial support groups) aimed at improving continuity of care.
- Strengthen healthcare providers' training on the evaluation and management of severe opportunistic infections in children.
- Ensure continuous availability of antiretroviral drugs and preventive treatments (cotrimoxazole, antifungals, antituberculosis drugs) across all treatment centers.
- Promote intersectoral collaboration (health, education, social protection) to reduce geographic, financial, and social barriers to medical follow-up.

For the community and families

- Raise awareness among parents, guardians, and extended families on the importance of early HIV screening and continuous care for infected children.
- Combat stigma and social rejection to encourage family adherence to healthcare services.
- Promote the establishment of family support networks to share experiences and strengthen resilience in the face.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no conflict of interest to disclose.

Statement of informed consent

Written informed consent was obtained from all individual participants and/or their legal guardians prior to inclusion in the study.

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