Original Article

Prevalence, Pattern, and Predictors of Opportunistic Infections in HIV-Infected Children on Antiretroviral Therapy: A Cross-Sectional Study in Plateau State, Nigeria

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ABSTRACT

Among children living with Human Immunodeficiency Virus (CLHIV), opportunistic infections (OIs) are a leading cause of morbidity and mortality, especially in sub-Saharan Africa where some of the children with HIV present with advanced HIV disease (AHD)-defined as CD4 count <200cells/µL or WHO clinical stage 3 or 4, or severe immunosuppression in children <5 years. Despite significant scale-up of antiretroviral therapy (ART), data on OI burden in North-Central Nigeria are limited, particularly in paediatric age group. We determined the prevalence, pattern, and independent risk factors for OIs among CLHIV in Plateau State, Nigeria. This descriptive cross-sectional study enrolled 404 HIV infected children aged 6 weeks to 18 years from 12 health facilities in Plateau State in 2017 using multistage sampling. Data on socio-demographics, clinical characteristics, ART and cotrimoxazole preventive therapy (CPT) adherence, CD4 counts, and hemoglobin were collected. Bivariate and multivariate logistic regression was used to identify independent predictors of OIs. The prevalence of any OI was 56.4% (228/404). Pulmonary tuberculosis (PTB) was the most common (31.7%, 128/404), followed by oral candidiasis (9.9%, 40/404), bacterial pneumonia (9.4%, 38/404), and sepsis (6.4%, 26/404). On multivariable analysis, female sex ((AOR = 2.70, 95% CI: 1.41–5.26, p = 0.003), orphan status (AOR = 2.82, 95% CI: 1.49–5.31, p = 0.001), duration of CPT less than two years (AOR = 4.24, 95% CI: 1.66–10.86, p = 0.003), and CD4 count <200 cells/µL (AOR = 5.84, 95% CI: 2.39–14.26, p < 0.001) emerged as independent predictors of OIs. The prevalence of OIs among HIV-infected children in Plateau State remains high, with PTB predominating. The key predictors of OIs were short CPT duration, severe immunosuppression, female sex, and orphanhood. These findings support the need for early ART initiation, sustained CPT adherence, targeted psychosocial support for orphans, and routine immunologic monitoring to reduce OI burden in this vulnerable population.

Keywords: Advance HIV disease, Children, Nigeria, Opportunistic infections, Prevalence, Risk factors.

INTRODUCTION

Opportunistic infections (OIs) are infections caused by bacterial, viral, fungal or protozoan pathogens that exploit a host compromised immune system.[1] Among children living with HIV (CLHIV), OIs remain a leading cause of hospital admission and death particularly in resource-poor settings where late diagnosis and delayed treatment initiation are common.[2,3] OIs exploit the host's compromised immune system, leading to a cycle of morbidity, malnutrition, and accelerated disease progression.[4]

The concept of advanced HIV (AHD) became prominent in the recent WHO guidelines. AHD is defined as CD4 <200cells/µL or WHO clinical stage 3 or 4 in children ≥5 years, and CD4<200cells/µL or WHO stage ¾ or severe immunosuppression in children <5 years.[5] Children with AHD face substantially elevated risks of OIs, hospitalization, and mortality even after ART initiation.[6,7] In 2022, approximately 1.29 million children worldwide were living with AHD, with the highest burden concentrated in sub-Saharan Africa.[8]

Evidence has shown that introduction of combination ART has dramatically reduced AIDS-related OIs and mortality in high-income countries.[9] However, these gains lag across sub-Saharan Africa, where late diagnosis, limited access to routine immunologic monitoring, and challenges with adherence to both ART and prophylactic therapies persist,[5,10] compounded by political and economic hardship. Nigeria has the highest burden of HIV globally, accounting for a significant proportion of new infant

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infections worldwide.[11] The North-Central region, including Plateau State, has historically reported elevated HIV prevalence, yet region-specific data on OIs in children remain scarce.

Children face unique risks for opportunistic infections compared to adults, as most infections often reflect primary acquisition of pathogens rather than reactivation of latent disease. This often leads to different clinical manifestations and greater severity.[12] Furthermore, factors such as orphanhood, poverty, malnutrition, and caregiver-related barriers to adherence place HIV-infected children at greater risk for OIs and AHD progression.[13,14]

Cotrimoxazole preventive therapy (CPT) is a cost-effective intervention that reduces OI-related mortality by up to 43% in CLHIV, irrespective of age or CD4 count.[15] The landmark CHAP trial in Zambia provided definitive evidence for CPT's efficacy[16], and the World Health Organization (WHO) recommends it as an integral part of the HIV care package in resource-limited settings, including for children with AHD. Despite this, CPT adherence is often suboptimal, and its protective effect can be compromised by drug resistance or inconsistent use, a common occurrence in other children and adolescents.[18,19]

Previous studies from Nigeria have reported varying OI prevalence, ranging from 42.4% in hospitalized children in Sagamu[20] to 61.7% in a mixed-age population in Kebbi State.[21] However, many studies included only hospitalized patients (introducing selection bias) or combined adults and children, limiting their generalizability to outpatient pediatric populations. Furthermore, few have systematically evaluated independent predictors of OIs among children receiving routine care in North-Central Nigeria, particularly in the context of AHD.

This study, therefore, aimed to:

(1) determine the prevalence and pattern of common OIs among HIV-infected children attending health facilities in Plateau State, Nigeria, and

(2) identify the independent sociodemographic and clinical risk factors associated with OI development, with particular attention to markers of advance HIV disease.

MATERIALS AND METHODS

Study Design and Setting

We conducted a descriptive cross-sectional study between March and September 2017 in Plateau State, North-Central Nigeria. The state has an estimated population of 3.5 million across 17 Local Government Areas (LGAs). At the time of the study, 24 health facilities provided comprehensive HIV care, including ART, CPT, CD4 count monitoring, and psychosocial support. Twelve facilities were randomly selected for inclusion.

Study Population

The source population was all CLHIV aged six weeks to 18 years registered for care at the selected facilities.

Inclusion criteria were:

(1) confirmed HIV-positive status (positive DNA PCR for children <18 months, or two sequential rapid tests for those ≥18 months), (2) age 6 weeks to 18 years, and (3) children with caregivers providing written informed consent. Children with acute, life-threatening illnesses requiring emergency intervention were excluded.

Sample Size and Sampling

Sample size was calculated using Fisher's formula, assuming a 42.4% OI prevalence from a prior Nigerian study[20], a 95% confidence level, a 5% margin of error, and a 10% non-response rate, yielding a target of 413 participants. A multistage sampling technique was used: (1) 12 health facilities were randomly selected from 24; (2) a proportionate allocation of participants was assigned to each facility based on its registered pediatric HIV caseload; (3) within each facility, participants were selected via systematic random sampling from the clinic register.

Data Collection

Data were collected by the principal investigator and three trained medical doctors using a structured case record form. A face-to-face interview with the caregiver captured sociodemographic data (age, sex, orphan status, socioeconomic status [SES]), clinical history (ART and CPT start dates, adherence), and anthropometric measurements. A complete physical examination was performed to identify signs of OIs.

SES was classified using the Olusanya method, combining paternal occupation and maternal education. ART/CPT adherence was assessed by caregiver 30-day recall, with ≥95% of prescribed doses taken defined as "good adherence." Anthropometric z-scores (weight-for-age, height-for-age, BMI-for-age) were calculated using WHO Anthro software. Stunting was defined as height-for-age z-score < -2.0.

Laboratory Methods

Most recent CD4 count (Partec CyFlow® cytometer) and hemoglobin/PCV were gotten from the records or a repeat done when necessary. CD4 counts were categorized using WHO pediatric thresholds: severe immunosuppression (<200 cells/μL), moderate (200-349 cells/μL), mild (350-499 cells/μL), and normal (≥500 cells/μL).[1] children with CD4 <200cells/μL were classified as having AHD per current WHO criteria.

Diagnostic Criteria for Opportunistic Infections

OIs were diagnosed using standardized national and international guidelines. Diagnoses based solely on clinical grounds required agreement between two independent physicians.

Pulmonary Tuberculosis (PTB): At least one of: (a) Acid-fast bacilli on sputum smear or GeneXpert positive; (b) Chest X-ray features compatible with TB (hilar lymphadenopathy, miliary pattern, cavity) plus compatible symptoms (cough >2 weeks, fever, night sweats, weight loss).

Oral Candidiasis: Clinical identification of creamy white plaques on oral mucosa, confirmed by microscopy of an oropharyngeal swab.

Bacterial Pneumonia: Acute fever, cough, or difficulty breathing with tachypnea and chest X-ray infiltrates.

Sepsis: Presence of at least two systemic inflammatory response syndrome (SIRS) criteria (temperature >38°C or <36°C, tachycardia, tachypnoea, abnormal white blood cell count) in the setting of a suspected or proven infection.

Other OIs (Herpes zoster, molluscum contagiosum, tinea capitis, etc.): Diagnosed based on characteristic clinical findings.

Statistical Analysis

Data were analyzed using SPSS version 25. Categorical

variables were summarized as frequencies and percentages; continuous variables as means (standard deviation) or medians (interquartile range). Bivariate associations between OI status and potential risk factors were tested using Pearson's chi-square or Fisher's exact test. Variables with $p < 0.10$ in bivariate analysis were entered into a multivariable binary logistic regression model to identify independent predictors of OIs. Adjusted odds ratios (AOR) with 95% confidence intervals (CI) were calculated. A two-tailed p-value < 0.05 was considered statistically significant.

Ethical Considerations

Ethical approval was obtained from the Research and Ethics Committee of Jos University Teaching Hospital (JUTH/RS/HREC/45/2017) and the Plateau State Healthcare Board. Written informed consent was obtained from parents/legal guardians, and assent from children ≥7 years. Confidentiality was maintained using unique study IDs. Children diagnosed with OIs received appropriate treatment per national guidelines.

Results

Participant Characteristics

A total of 404 HIV-infected children participated (97.8% response rate). The mean age was 10.7 ± 4.0 years, with the majority aged 10-14 years (45.5%, n=184). Females comprised 60.4% of the sample. Low socioeconomic status was recorded in 62.8%(n=254) of participants, and 55.0% (n=222) were orphans. Most participants (97.0%) were on ART, with 81.2% reporting good adherence. The median CD4 count was 356 cells/µL (IQR: 210–512), and 36.9% of children had severe immunosuppression (CD4 < 200 cells/µL), meeting criteria for AHD. See Table 1

Prevalence and Pattern of Opportunistic Infections

The overall prevalence of at least one OI was 56.4% (228/404). Among children with OIs, 85.1% (194/228) had a single OI, 11.4% (26/228) had two, 2.6% (6/228) had three, and 0.9% (2/228) had four concurrent OIs.

Pulmonary tuberculosis (PTB) was the most common OI, affecting 31.7% (128/404) of all participants. Oral candidiasis (9.9%, 40/404), bacterial pneumonia (9.4%, 38/404) and sepsis (6.4%,26/404) were the next most frequent. The full spectrum of OIs is detailed in Table 2.

Age-Specific Distribution of Major OIs

The distribution of OIs varied significantly by age ($p < 0.001$) (Table 3). Oral candidiasis and bacterial pneumonia/sepsis were most common in children under 5 years. Dermatological infections (tinea, herpes zoster) became more prominent in school-aged children (5-14 years). Tuberculosis (PTB and DTB combined) showed an increasing trend with age, peaking in adolescents over 14 years (25.8%). See Table 3

CD4 Count and Advanced HIV Disease as Predictors of OIs

A strong, inverse correlation was observed between CD4 count and OI occurrence. The prevalence of any OI was 92.6% among children with severe immunosuppression (CD4 <200 cells/µL, consistent with AHD) compared to only 37.1% among those with normal CD4 counts (≥500 cells/µL) ($p < 0.001$) (Table 4). The median CD4 count was significantly lower in children with OIs (198 cells/µL, IQR: 98-310) than in those without OIs (412 cells/µL, IQR: 301-588), $p < 0.001$. See Table 4.

Independent Predictors of Opportunistic Infections

On multivariable logistic regression, four factors emerged as independent predictors of OIs (Table 5). Severe immunosuppression (CD4 <200 cells/µL) was the strongest predictor (AOR = 5.84, 95% CI: 2.39-14.26, $p < 0.001$), followed by CPT use for less than two years (AOR = 4.24, 95% CI: 1.66-10.86, $p = 0.003$). Female sex (AOR 2.70; 95% CI: 1.41–5.26; $p = 0.003$).) and orphan status (AOR = 2.82, 95% CI: 1.49-5.31, $p = 0.001$) were also associated with high odds of OIs. Age and socioeconomic status were not significant in the final model. See Table 5

Table 1: Baseline Characteristics of HIV-Infected Children in Plateau State, Nigeria (N=404)

Characteristic	Category	Frequency (n)	Percentage (%)
Age Group (years)	<5	40	9.9
	5-9	92	22.8
	10-14	184	45.5
	≥15	88	21.8
Sex	Male	160	39.6
	Female	244	60.4
Orphan Status	Yes	222	55.0
	No	182	45.0
Socioeconomic Status	High/Middle	150	37.2
	Low	254	62.8
On ART	Yes	392	97.0
	No	12	3.0
ART Adherence (past month)	≥95% (Good)	328	81.2
	<95% (Poor)	76	18.8
On CPT	Yes	396	98.0
	No	8	2.0
CPT Duration (years)	<2	48	11.9
	≥2	356	88.1
CD4 Count (cells/µL)	<200 (Severe)	149	36.9
	200-349 (Moderate)	84	20.8
	350-499 (Mild)	50	12.4
	≥500 (Normal)	35	8.7
	Missing	86	21.2

Table 2: Spectrum of Opportunistic Infections Among HIV-Infected Children (N=404)

Opportunistic Infection	Frequency (n)*	Percentage of all children (%)
Pulmonary Tuberculosis (PTB)	128	31.7
Oral Candidiasis	40	9.9
Bacterial Pneumonia	38	9.4
Sepsis	26	6.4
Tinea Capitis	18	4.5
Disseminated Tuberculosis (DTB)	12	2.9
Verruca Plana	12	2.9
Herpes Zoster	6	1.5
Herpes Simplex	6	1.5
Molluscum Contagiosum	6	1.5
Varicella	4	1.0
Measles	2	0.5
Genital Herpes	2	0.5
***Note:** Children could have more than one OI. The total number of OI events is >228.		

Table 3: Distribution of Major OIs by Age Group Among HIV-Infected Children (N=404)

Age Group (years)	OI Type	Frequency (n)	Percentage within Age Group (%)	p-value**
0-4 (n=40)	Oral Candidiasis	12	30.0	
	Bacterial Pneumonia/Sepsis	8	20.0	
	Tuberculosis (PTB/DTB)	4	10.0	<0.001
5-9 (n=92)	Tinea Capitis	32	34.8	

	Tuberculosis	20	21.7
	Oral Candidiasis	10	10.9
10-14 (n=184)	Tinea Capitis	58	31.5
	Tuberculosis	34	18.5
	Herpes Zoster	14	7.6
≥15 (n=88)	Tuberculosis	22	25.0
	Tinea Capitis	18	20.5
	Herpes Zoster	10	11.4

Column percentages (within age group). Only the top three OIs per age group are shown.
Chi-square test for association between age group and presence of any major OI.

Table 4: Association Between CD4 Count Category and Opportunistic Infections

CD4 Count Category (cells/µL)	Any OI Present (n)	No OI (n)	Prevalence of OI (%)	Crude OR (95% CI)
<200 (Severe)	138	11	92.6	20.1 (9.2-44.1)
200-349 (Moderate)	68	16	81.0	6.8 (3.2-14.5)
350-499 (Mild)	32	18	64.0	2.9 (1.4-6.1)
≥500 (Normal)	13	22	37.1	Reference

Missing CD4 data (n=86) excluded from this table.

Table 5: Multivariable Analysis of Factors Associated with Opportunistic Infections

Variable	Category	AOR	95% CI	p-value
Sex	Male	Reference		
	Female	2.70	1.41 – 5.26	0.003
Orphan Status	No	Reference		
	Yes	2.82	1.49 – 5.31	0.001
CPT Duration	≥2 years	Reference		
	<2 years	4.24	1.66 – 10.86	0.003
CD4 Count	≥500 cells/µL	Reference		
	350-499 cells/µL	2.51	0.94 – 6.70	0.066
	200-349 cells/µL	5.97	1.90 – 18.75	0.002
	<200 cells/µL	5.84	2.39 – 14.26	<0.001

AOR: Adjusted Odds Ratio; CI: Confidence Interval. Model adjusted for all variables in the table plus age and anemia.

DISCUSSION

This study provides contemporary, facility-based data on OIs among CLHIV in North-Central Nigeria. The key findings- a high prevalence of OIs (56.4%), a predominance of PTB, strong inverse correlation with CD4 count, and independent predictors including short CPT duration, severe immunosuppression, female sex, and orphanhood - have important clinical and public health implications.

Prevalence and Pattern

The 56.4% prevalence of OIs in this largely ambulatory study population is substantial and highlights the ongoing vulnerability of CLHIV despite high (97%) ART coverage. This figure is comparable to the 54.0% prevalence reported in Indian CLHIV,[22] and the 61.7% reported in a Nigerian mixed-age cohort.[21] It is, however, higher than the 42.4% found in a hospitalized Nigerian pediatric study,[20] likely because the hospitalized study captured a narrower window of severe, acute OIs, whereas our cross-sectional design captured both acute and chronic, indolent OIs (e.g., tinea, verruca plana) seen in routine care.

While comparator groups (HIV-uninfected children or HIV-infected adults) were not included in this study, the OIs prevalence observed substantially exceeds background community rate – particularly the 31.7% PTB prevalence, which far exceeds the <2% background rate in Nigeria children under 15 years.[23] The dominance of PTB (31.7%) is a critical finding. Nigeria is a high TB-burden country, and HIV is the strongest risk factor for progression from latent *M. tuberculosis* infection to active disease.[23] The high proportion of orphans (55.0%) and low SES (62.8%) in our cohort likely facilitates household TB transmission.[24] This prevalence is alarmingly similar to the 32% rate reported in Jos a decade earlier,[25] suggesting that TB control among CLHIV has not improved substantially.

Oral candidiasis (9.9%) was the second most common OI, but its prevalence was much lower than the 65-79% reported in studies focusing on younger children.[26,27] Our cohort's older mean age (10.7 years) and prolonged ART exposure likely explain this lower rate, as immune reconstitution reduces *Candida* colonization and disease.

Advanced HIV Disease and Independent Predictors of OIs

Severe immunosuppression (CD4 <200 cells/µL, AHD) was the strongest predictor of OIs (AOR 5.84). This finding is consistent with a large body of literature,[6,7] and validates the WHO's use of CD4 thresholds for identifying high-risk children and prioritizing AHD management.[1] The fact that 36.9% of our cohort had CD4 counts <200 cells/µL, despite most being on ART, suggest late diagnosis, prior treatment failure, or poor adherence - patterns characteristic of AHD in resource-limited setting.[8,10] The 2022 WHO consolidated guidelines emphasize enhanced package of care for children with AHD, including rapid ART initiation, intensified clinical and laboratory monitoring and opportunistic infection prophylaxis.[1] This study strongly support these recommendations.

The strong association between CPT use for ≥2 years (AOR 0.24) and reduced OIs, which potentially subject to reverse causation, agrees with established longitudinal evidence of CPT efficacy and represents a key programmatic finding. This aligns with the CHAP trial and subsequent studies demonstrating that sustained CPT reduces bacterial infections, malaria, and mortality in CLHIV.[15,16,29] The increased risk associated with shorter CPT duration (<2 years) suggests that many children either started CPT late (e.g., at the time of OI diagnosis) or had inconsistent adherence. Continued indefinite CPT, as recommended by WHO for resource-limited settings, is supported by these data.[17,30]

Female sex was associated with higher odds of OIs (AOR 2.70). While some studies show no sex-based difference in pediatric OIs, others suggest immunological or adherence

differences.[31] Girls may have better ART adherence due to caregiving roles or clinic attendance patterns.[32] Alternatively, this could be a chance finding due to the higher proportion of females (60.4%) in our sample or this may reflect social, behavioural or care- access differences rather than biological susceptibility. Similarly, orphanhood had increased odds (AOR 2.81). This agrees with the view that social vulnerability affects HIV outcomes through delayed care-seeking, unstable caregiving, poor nutrition, treatment interruption and reduced adherence support [13,14 33] despite older orphans in this study.

LIMITATIONS

This study has some limitations. First, the cross-sectional design prevents causal inference. Second, the diagnosis of PTB in children is very difficult; we used a composite of clinical, radiological, and microbiological criteria, but some misclassification is possible. Third, self-reported adherence is subject to recall and social desirability bias. Fourth, we did not assess for *Pneumocystis jirovecii* pneumonia or cytomegalovirus, which require specialized testing that were not available. Fifth, the study was conducted in 2017; while the core findings on risk factors remain relevant, the ART landscape has evolved with wider access to dolutegravir.

CONCLUSION

The prevalence of opportunistic infections among HIV-infected children in Plateau State, Nigeria, remains high at 56.4%, with pulmonary tuberculosis as the predominant infection. Short duration of cotrimoxazole preventive therapy (<2 years), severe immunosuppression (CD4 <200 cells/µL), and being female or orphaned were independent risk factors. These findings show the importance of early ART initiation, sustained CPT adherence, routine immunologic monitoring, and targeted psychosocial support for vulnerable children. Intensified efforts in TB/HIV integration, PMTCT, and adherence support are urgently needed to reduce the OI burden and improve outcomes for this vulnerable population.

RECOMMENDATIONS

Our findings support several actionable recommendations. First, routine TB screening (e.g., WHO four-symptom screen) at every clinical encounter and provision of isoniazid preventive therapy (IPT) to all CLHIV without active TB should be prioritized. Second, CPT should be initiated at HIV diagnosis and continued indefinitely, with intensive adherence support for children and families, particularly those with AHD.[17] Third, regular CD4 monitoring remains essential to identify children at highest OI risk who may require more frequent visits, secondary prophylaxis or AHD-specific interventions.[6,7] Fourth, the high orphan rate calls for integration of psychosocial and nutritional support into HIV care programmes. Finally, this study underscores the urgent need to strengthen prevention of mother-to-child transmission (PMTCT) to reduce the number of new pediatric HIV infections and consequently AHD.[11]

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