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Opportunistic Infections Amongst HIV Infected Children and Correlation with Who Clinical Staging in Owerri, South East Nigeria

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Abstract

Background: Opportunistic infections are the most common cause of death among children living with Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome. They take advantage of the weakened immune system and cause devastating illnesses. Studies with respect to the prevalence of opportunistic infections in HIV infected Nigerian children are very limited. This study aimed to determine the prevalence of opportunistic infections in HIV infected children at Federal University Teaching Hospital Owerri and to correlate it with World Health Organization clinical staging. ***Methods:*** 100 HIV infected children aged 2-16 years were recruited consecutively at the pediatric infectious disease clinic of the Federal University Teaching Hospital Owerri. Diagnostic criteria for opportunistic infections in HIV infected children were based on the hospital's standard clinical protocols aligned with national and international guidelines. They were classified into World Health Organization clinical staging. They were further categorized based on CD4 count values using World Health Organization classification of immune deficiency. ***Result:*** The mean age of participants was 9.73 years. Majority of participants (59%) were in World Health Organization Clinical Stage I and (1%) was in stage IV. Pneumonia (68%) was the most common opportunistic infection recorded among participants. Fifty seven percent of subjects had CD4 counts > 500cells/mm3 while 17% had CD4 counts < 200cells/mm.3 There was significant association between opportunistic infections and WHO clinical Staging. Place of residence and socioeconomic status were found to be significant risk factors for development of opportunistic infections. ***Conclusion:*** In this study, the prevalence of Opportunistic infections in HIV infected children at Federal University Teaching Hospital Owerri remained high. Opportunistic Infections majorly occurred with worsening World Health Organisation clinical staging, low socio economic status and inhabitants of rural areas. We recommend consideration be given to early screening and treatment of Opportunistic Infections in HIV infected children.

Keywords: ***Opportunistic infections, HIV, Children, Immune suppression.***

Background

The global Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) epidemic have become one of the greatest threats to human health and development, particularly in less developed countries [1]. Nigeria has the second largest HIV epidemic following South Africa and the highest burden of pediatric HIV and AIDS in the world [2]. As at 2021, the Nigerian national prevalence of HIV infection is estimated at 1.4%. Twelve percent of people living with HIV infection are children aged 0 to 14 years, while 8% are adolescents aged 10 to 19 years [3]. Profound immune suppression occurs in HIV infected children. The hallmark of this process is the depletion of CD4+ lymphocytes, which predisposes the patient to develop a variety of opportunistic infections [4].

Opportunistic infections (OIs) are the most common cause of death among children living with HIV/AIDS. They are called opportunistic because they take advantage of the weakened immune system and cause devastating illnesses. Common OIs in HIV infected children include Tuberculosis, Candida, Pneumocystis jirovecii Pneumonia, chronic diarrhea, invasive and recurrent fungi, cryptosporidiosis, cytomegalovirus, varicella zoster virus, Herpes simplex virus and Toxoplasmosis. In children, OIs have a more

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aggressive course compared to adults [5]. The World Health Organization (WHO) recommends a range of medical interventions to reduce OIs. This includes chemoprophylaxis, immunization, reduction of exposure and early initiation of highly active anti-retroviral therapy (HAART) [6]. Failure of early treatment of OIs in people living with HIV (PLHIV) results to poor quality of life, impaired patient's response to anti-retroviral therapy, increased disease progression and increased medical cost [7,8].

Most reports on the magnitude of OIs in HIV infected children are from North America and Europe [9]. Ravichandra *et al* [10] reported a 56% prevalence of opportunistic infections in HIV infected children in India.

The burden of OIs in HIV infected children in low and middle-income countries including Nigeria are poorly documented. However, Imade PE and Eghafona NO [11] reported that malaria parasite infection has the highest prevalence among OIs in HIV infected children in Benin City Nigeria. This study therefore was undertaken to determine the prevalence of OIs in HIV infected children attending the pediatric infectious disease clinic at Federal University Teaching Hospital Owerri. Results obtained from this study will add to existing data on burden of OIs in HIV infected children. It will also serve as a reference for clinicians whom will partake in similar research.

Objectives

To determine the prevalence of opportunistic infections in HIV infected children at Federal University Teaching Hospital Owerri.
To correlate opportunistic infections with WHO clinical staging of HIV infection
To determine the socio demographic factors associated with opportunistic infections

Methods

Study setting
Owerri is the capital of Imo State in the South East Geopolitical Zone of Nigeria [12]. Imo state has an estimated population of about 4,927,563 with about 403,425 people living in Owerri [13] Federal University teaching hospital Owerri is the major tertiary health care facility in the state which serves as a referral centre for those living in Owerri and the surrounding towns as well as neighbouring states of Abia, Rivers and Anambra.

Study design
A hospital based cross-sectional study.

Study period
Conducted from October 2018 to January 2019 at the paediatric infectious disease clinic of Federal University teaching hospital Owerri Imo State.

Inclusion criteria
All HIV positive children aged 2-16 years whose parents consented to the study.

Exclusion criteria
HIV positive children whose parents declined consent.

Study population
HIV positive children aged 2-16years.

Sampling procedure
100 HIV positive children that met the inclusion criteria were enrolled consecutively.

Data collection
A structured interviewer administered questionnaire was developed and administered to parents and guardians, to obtain child's demographic data, mode of HIV transmission, current or past history of opportunistic infections, route of HIV transmission. Based on clinical presentations, the children were categorized into various WHO clinical staging. Diagnostic criteria for opportunistic infections in HIV infected children were based on the hospital's standard clinical protocols aligned with national and international guidelines. CD4 count was also determined using CY flow methods. Other investigations done include full blood count, sputum for AFB, chest x-ray, mantoux, blood culture, stool MCS, urine MCS, ultrasound scan of abdomen/chest, cerebrospinal fluid analysis and culture sensitivity. Investigations were done according to clinical presentation of patients.

Variables
The primary outcome of interest was prevalence of opportunistic infections in HIV infected children. The primary exposures and predictors included WHO clinical staging, low socio-economic status, place of inhabitant. These variables were selected based on previously published research works suggesting they influence the likelihood of opportunistic infections in HIV infected children. Diagnostic criteria for opportunistic infections in HIV infected children were based on the hospital's standard clinical protocols aligned with national and international guidelines. These criteria were used to classify the primary diagnosis and assess the presenting condition's severity.

Bias
Several strategies were employed to minimize bias in the study. Selection bias was addressed by applying strict inclusion and exclusion criteria, ensuring that the study population was representative of the broader pediatric population seen in the HIV clinic. Information bias was minimized through standardized data collection methods and the cross-verification of data sources.

Data analysis
The data collected was coded and imputed into Statistical Package for Social Sciences (SPSS) version 20.0. Frequency tables and figures were used to present relevant variables.

Quantitative variables were used to summarize descriptive statistics (mean and standard deviation, age and social class). Qualitative variables were summarized as proportions. The Chi-square test was used to compare associations between proportions.

Ethical approval
Ethical approval was obtained from the ethics committee of Federal Medical Center Owerri (FMC/OW/IIREC/182). Informed consent of the parents and assent from children 7 years and above were obtained for the study and confidentiality maintained.

Results

A total of 100 patients were recruited from October 2018 to January 2019. Fifty-one were females while 49 were males. Majority 44 (44%) are from middle socioeconomic class. Hundred percent of study population were Christians100 (100%) and 65(65%) are rural dwellers. Majority of participants (57) had CD4 cell count above 500 cells/mm3 and (17) have CD4 below 200cell/mm3 as shown in Table I.

Of the 100 subjects, 59 were in WHO clinical Stage 1 and only 1 was in stage 4. Subjects on ART were 93 while 7 were HAART naïve. It was observed that 20(63%) participants had

Pneumonia, 5(16%) had oral thrush, 4(12%) had Pulmonary Tuberculosis and 3(9%) people had herpes zoster. There was a significant association between PTB, Pneumonia, Oral Thrush and WHO clinical Staging as depicted in Table II.

The WHO clinical staging of HIV and place of residence were found to be significant risk factors for development of opportunistic infections. Of all opportunistic infections, 71% (23) occurred among rural dwellers and this was statistically significant, (p-value 0.003). Similarly prevalence of opportunistic infections increased with worsening WHO stage and this was statistically significant (p-value 0.01). Prevalence of all the studied infections increased with lower social class. This was not statistically significant (p-value 0.92) as shown in Table III.

Table 1: Socio demographic Characteristics and CD4 levels of Participants

Variable	**Frequency**	**Percent (%)**
Gender		
Female	51	51
Male	49	49
Religion		
Christianity	100	100
Social Class		
Upper	20	20
Middle	44	44
Lower	36	36
Place of Residence		
Rural	65	65
Urban	35	35
CD4 Cell level of Participants	**Frequency**	**Percent**
<200	17	17
200-349	13	13
350 -499	13	13
>500	57	57
Total	**100**	**100**
There were slightly more females than males, all participants were Christians, majority were from middle class, and lived in rural areas. Furthermore, 57% of study subjects have adequate immunity while 17% were immune suppressed.		

Table II: Who Staging, Use of HAART, Opportunistic infection and Correlation between opportunistic infections and WHO Staging

WHO Staging		
Variables	**Frequency**	**Percent**
1	59	59
2	16	16
3	24	24
4	1	1
Total	**100**	**100**
Use of HAART	**Frequency**	**Percent**
Yes	93	93
No	7	7
Total	**100**	**100**
Opportunistic infection	**Number**	**Percentage**
Pneumonia	20	63%
Oral thrush	5	16%
PTB	4	12%
Herpez zoster	3	9%
Correlation between opportunistic infections and WHO Staging		
Variables	**WHO Staging**	
	Rho	**p-value**
PTB	0.30	0.003*
Herpes Zoster	0.16	0.11
Pneumonia	0.73	<0.001
Oral thrush	0.33	0.001*
Majority of study participants (51%) were in WHO stage one while only 1 patient was in WHO stage 4. 93% were on antiretroviral drugs while 7 patients were HAART naïve. 63% had pneumonia, the second most common opportunistic infection was oral thrush followed by pulmonary TB, herpes zoster was the least common. There was significant association between PTB, Herpes zoster, Pneumonia, oral thrush and WHO clinical staging of HIV.		

rho Spearman Correlation coefficient

Table III: Association between Risk factors and Development of Opportunistic Infections

Variables	Opportunistic Infections n (%)				Total	$\chi 2^{¥}$	p-value
Domestic Animals	**Herpes Zoster**	**PTB**	**Bacterial Pneumonia**	**Oral Thrush**			
Fowl/Ducks/Turkey	1(50.0)	1(100.0)	8(88.9)	1(100.0)	11(84.6)		
Goats/Sheep	1(50.0)	0	0	0	1 (7.7)	4.88	0.55
Dogs	0	0	1(11.1)	0	1 (7.7)		
Total	**2(100.0)**	**1(100.0)**	**9(100.0)**	**1(100.0)**	**13(100.0)**		
Place of Residence							
Rural	2 (66.6)	4(100.0)	14 (80.0)	3 (60.0)	23(71.9)		
Urban	1 (33.3)	0	6 (20.0)	2 (40.0)	9 (28.1)	14.08	0.003
Total	**3 (100.0)**	**4(100.0)**	**20 (100.0)**	**5 (100.)**	**32(100.0)**		
WHO Stage							
1	0	0	0	0	0		
2	2 (33.3)	0	0	0	2 (6.3)	11.14	0.01
3	1 (66.6)	4 (100.0)	20 (100.0)	5(100.0)	30 (93.7)		
4	0	0	0	0	0		
Total	**3 (100.0)**	**4 (100.0)**	**20 (100.0)**	**5(100.0)**	**32 (100.0)**		
Social Class							
Upper	0	0	0	0	0		
Middle	0	0	2 (14.3%)	1 (25.0)	3 (13.0)	2.04	0.92
Lower	3 (100.0)	2 (100.0)	12 (85.7)	3 (75.0)	20 (87.0)		
Total	**3 (100.0)**	**2 (100.0)**	**14(100.0)**	**4 (100.0)**	**23(100.0)**		
Opportunistic infections were more common in those that lived in rural areas, low socio economic class, increasing WHO clinical staging and those whose parents reared fowls.							

¥ Likelihood ratio, Table has many small variables (less than 5) as such odds ratio will be misleading

Discussion

The prevalence of opportunistic infections in HIV infected children aged 2-16years attending the HIV care/treatment center of Federal Teaching Hospital Owerri South East Nigeria was 32%. This finding is comparable to the 31.6% prevalence of OIs in HIV infected children in the study by Mamaru et al in Ethopia [14]. The prevalence of OIs in this study was also similar to the 28.8 incidence of OIs per 100 HIV infected children in an Asian study by Wasana Prasitsuebsai *et al.* [15].

However, the prevalence of OIs in this study is lower than the 56% prevalence of OIs obtained in the Indian study by Ravichandra *et al.* [10]. The difference in prevalence may be due to the fact that majority of patients in the Indian study were severely immune compromised, while majority of participants in this study were not severely immune compromised and were on HAART. Also, 98% of study participants washed hands regularly before a meal, 92% washed fruits regularly before eating and 75% drank water from bore hole. These simple acts of hygiene would have drastically reduced the risk of contracting infections.

Pneumonia was the most common opportunistic infection (63%) followed by oral thrush (16%). Tuberculosis and herpes zoster was seen in 12% and 9% of children respectively. Similarly, a study from Latin America, [16] revealed that bacterial pneumonia is the most common OI. However, in contrast to our study, Imade E and Eghafona NO (11) reported that malaria parasite infection has the highest prevalence among OIs in HIV infected children in Benin City Nigeria. This difference may be due to the fact that our study was conducted during the dry season while the environmental condition of the locality of the Benin study and the low immune status of the children may have resulted to a high prevalence of malaria infection.

This study also showed a significant association between PTB, Pneumonia, Oral Thrush and WHO clinical Staging. Place of residence and socioeconomic status were found to be significant risk factors for development of opportunistic infections. Of all opportunistic infections, 71% [23] occurred among rural dwellers. This may be due to the fact that rural dwellers have poor access to prompt health care as many specialized hospitals are located in big cities. Similarly, prevalence of opportunistic infections increased with worsening WHO stage because patients in this stage are severly immune suppressed. Prevalence of all the studied infections increased with lower social class. This may be due to the fact that indigent patients are unable to provide adequate nutrition, hence are unable to build the right immunity to fight infections.

Interpretation of results

This study depicts the fact that there is a high rate of opportunistic infections in HIV infected children. They prey on the immune suppression of HIV infected children and cause debilitating illness. Therefore physicians managing HIV infected children should look out for opportunistic infections especially in those with worsening WHO clinical staging, those from low socioeconomic background and those in rural areas. This is due to the fact that HIV infected children with these risk factors have very low immunity, with malnutrition due to poverty and poor access to health care. Also, early diagnosis and prompt treatment leads to better outcomes. Furthermore, a multicenter study would give a broader view of opportunistic infections in HIV infected children.

Generalisability: This is a single center study, a multicenter study would have given the results a broader look.

Future research: Multi center study in patients with very low CD4 counts.

Limitations of study

This is a single center study. A multi center study may provide a broader view of OIs in HIV infected children.

Conclusion

In this study, the prevalence of OIs in HIV infected children at FMC Owerri remained high. OIs majorly occurred with worsening WHO clinical staging, low socioeconomic status and inhabitants of rural areas. We recommend consideration be given to early screening and treatment of OIs in HIV infected children.

What is already known on this topic

- Opportunistic infections are the most common cause of death among children living with HIV/AIDS.
- Opportunistic infections take advantage of the weakened immune system and cause devastating illnesses.
- Studies with respect to the prevalence of opportunistic infections in HIV infected Nigerian children are very limited.

What study adds

- The prevalence of OIs in HIV infected children at FUTH Owerri is high.
- OIs majorly occurred with worsening WHO clinical staging.
- OIs majorly occurred with low socioeconomic status and inhabitants of rural areas.

Declarations

Conflict of interest

Authors declare no conflict of interest.

UN's declaration of human right

All authors agree with UN's declaration of human right.

Author contributions

Chinelo Vivian Okeke: conceptualization of study, writing, expertise, review, data collection, data analysis, result interpretation.
Sampson Dayo Ejikunle: writing, review, result interpretation, exprtise
Bede Ikenna Nnolim: writing, review, result interpretation, data analysis.
Idabo Oghenetega: writing, review, data analysis
Ganiyat Yusuf: writing, review, data analysis
Maria- lauretta Orji: conceptualization, supervision, writing, expertise, review.

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