International Journal of Biomedical and Health Sciences
Vol. 4, No. 1, March 31, 2008
Printed in Nigeria

0794-4748/2008 $12.00 + 0.00

http://www.asopah.org

IJBHS 2007090/4102

Pattern of opportunistic infections and other co-morbidities among hospitalised children with HIV infection in Nigeria

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(Received October 13, 2007)

ABSTRACT: **Background:** The patterns of opportunistic infections (OIs) associated with HIV vary in different parts of the world. **Objective**: To define the pattern of opportunistic infections and other co-morbidities amongst hospitalised children with HIV infection in South-western Nigeria. **Method:** Hospital records of all paediatric admissions diagnosed with HIV infection in our hospital over a ten-year period were reviewed. Relevant data were extracted and analysed. **Results:** There were 33 cases of paediatric HIV/AIDS out of a total of 3,061 paediatric admissions during the study period. Male: Female ratio was 1:1.4 while mean (SD) age was 17.4 (23.2) months. 87.9 % of the patients were under-5 children. Fourteen (42.4%) patients presented with OIs, mainly oropharyngeal candidiasis and pulmonary tuberculosis. No patient was diagnosed with pneumocystis carinii pneumonia. Other commonly observed infections among the patients were septicaemia, chronic otitis media and gastro-enteritis in 8 (24.2%), 7 (21.2%) and 5 (15.2%) patients respectively. Protein-energy malnutrition and anemia were common co-morbidities. Mortality rate was 33.3% with septicaemia and pulmonary TB having the highest case fatality ratio. **Conclusion:** Oropharyngeal candidiasis and pulmonary tuberculosis are the commonest OIs that affect children with HIV infection in the south-western part of Nigeria while septicaemia is a major cause of death.

Key Words: Opportunistic infections, Paediatric HIV/AIDS, Nigerian children.

Introduction

The human immunodeficiency virus (HIV) has, as its main target, the immune system of an individual thereby causing functional abnormalities and progressive depletion of the T lymphocyte population, particularly the CD4+ component. This depletion occurs through various mechanisms, notably single-cell killing caused by intracellular accumulation of HIV DNA, inhibition of cell function, syncitium induction and giant cells' generation, and antibody-dependent cellular toxicity [1-3]. Other recognised mechanisms for immune depletion include auto-immune destruction resulting from cross-reactivity between components of viral envelope and MHC II antigens, and programmed cell death (apoptosis) [2-5]. Apart from cell depletion, HIV causes additional immunological defects which include CD4+ and CD8+ cell dysfunction, B-cell abnormalities, thymic dysfunction and autoimmune abnormalities [2,3].

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The destruction of the immune system by the virus results in opportunistic infection (OI), as well as an increased risk of auto-immune disease and malignancy [6]. Amongst paediatric patients, the most widely reported OIs include *Pneumocystis carinii* pneumonia (PCP), oropharyngeal candidiasis, pulmonary/ disseminated tuberculosis, and disseminated cytomegalovirus infection [7-12]. Whether these infections occur at the same frequency amongst Nigerian children with HIV infection has not been fully established. We therefore decided to review the clinical presentation of paediatric patients admitted with HIV infection in our hospital in order to define the pattern of OIs and other co-morbidities among them.

Materials and Methods

The study is a retrospective survey carried out at a teaching hospital located in the south-western part of Nigeria. All hospitalised paediatric patients that tested positive to HIV serological test between Jan. 1996 and Dec. 2005 were included in the study. In addition to being HIV positive, those that were under 18 months of age were required to meet the WHO criteria for the case-definition of paediatric HIV/AIDS [13] to be included in the study. The major features of this are failure to thrive or weight loss, chronic diarrhoea, (> one month) and prolonged fever (> one month). The minor features are generalized lymphadenopathy of at least 0.5cm, present in two or more sites, with bilateral lymph nodes counting as one site, oropharyngeal candidiasis, repeated common infections (otitis, pharyngitis etc), persistent cough (> one month), generalized dermatitis and confirmed maternal HIV. The presence of at least, two major features with at least two minor ones, in the absence of a known cause of immunosuppression is indicative of paediatric HIV infection.

The hospital records of the selected patients were reviewed and relevant data extracted for analysis. These included age and sex, body weight at presentation, presenting symptoms and physical findings, immunisation status, past medical history, maternal HIV status, relevant laboratory results, diagnosed medical conditions, outcome, and length of hospital stay.

HIV screening was done on each patient by two methods namely, the Immunocombs II HIV 1&2 Bispot test kit (Orgenics, France) and the Capillus HIV-1/HIV-2 kit (Cambridge diagnostics, Ireland). A test was considered positive only when the blood sample gave positive results with both test kits. The western blot confirmatory test was not done as it was not available in the hospital. For the same reason, HIV DNA PCR assays, RNA assays including viral load and other virologic studies could not be done. CD4+ count of the patients was also not done. Diagnosis of opportunistic infection was based on typical clinical features supported by laboratory evidence where possible.

Data analysis was conducted by means of SSPS version 10.0. Descriptive statistics including range, mean, standard deviation and percentages were computed.

Results

Out of a total of 3061 paediatric admissions during the study period, 33 (1.1%) patients met the selection criteria and were included in the study. There were 14 males and 19 females giving a M:F ratio of 1:1.4. Their ages ranged from 2 months to 120 months with a mean (SD) of 17.4 (23.2) months. Table 1 presents the age and sex distribution of the patients. Majority of the patients were under-5 children. Thirty-one (93.9 %) patients were infected with HIV1 strain while the remaining 2 (6.1%) tested positive for both HIV1and 2. None of the children was infected with HIV 2 alone. The Mean (SD) weight of the patients was 5.9 (3.1) kg and this was only 54.1% of the 10.9 kg expected for their mean age. Twenty three (69.7%) of the mothers tested positive to HIV thereby making vertical transmission the most likely route of infection in the children of these mothers. Three patients (9.1 %) had a past history of blood transfusion for anaemia and their mothers were HIV negative. In the remaining 7 patients, probable route of transmission could not be determined due to incomplete records.

A total of 14(42.4 %) patients presented with opportunistic infections. Oro-pharyngeal candidiasis was the most commonly observed OI accounting for 10(71.4%) cases while the remaining 4(28.6%) patients were diagnosed with pulmonary tuberculosis. Three (9.1%) patients had clinical and radiographic features

of acute bacterial pneumonia but none had bronchial lavage performed for the diagnosis of PCP. Other commonly observed co-morbidities of infective origin among the patients were septicaemia, chronic suppurative otitis media and gastroenteritis. These conditions were diagnosed in 8 (24.2 %), 7 (21.2 %) and 5 (15.2%) patients respectively [Table 2]. Fifteen (45.5%) patients had protein-energy malnutrition: 11 were marasmic, 3 had marasmic-kwashiorkor and only one had kwashiorkor. Diaper dermatitis was observed in 12 (36.4%) of the patients while 2 (6.1%) had pyoderma.

Table 1: age and sex distribution of HIV-infected patients

Age Group	Sex		Total
	Male	Female	No. (%)
0-12 months (infants)	6	8	14 (42.4)
13-60 months (pre-school)	5	10	15 (45.5)
61-120 months (school-aged)	3	1	4 (12.1)
Total	14	19	33 (100)

Table 2: Incidence of OIs and other co-morbidities among the patients (n =33).

Clinical entity	No. (%) of patients
Oro-pharyngeal candidiasis	10 (30.3)
Pulmonary tuberculosis	4 (12.1)
Septicaemia	8 (24.2)
Chronic Otitis	7 (21.2)
Gastroenteritis	5 (15.2)
Pneumonia	3 (9.1)
Protein-energy malnutrition	15 (45.5)
Dermatitis	14 (42.4)

Haematocrit level ranged from 10 to 40% with a mean (SD) of 24.8(8.4)%. Nine (27.3 %) patients presented with moderate to severe anemia, their packed cell volume being <21% thereby needing blood transfusion. Mean (SD) white blood cell (WBC) count was 9961(5774) /µL while mean (SD) lymphocyte count (TLC)was 3932 (2880)/µL. Table 3 shows further that erythrocyte sedimemtation rate (ESR) was generally elevated among the patients.

There were 11 mortalities amounting to 33.3 % of all patients. Case fatality rate was highest for Septicaemia, followed by TB and pneumonia as shown in Table 4. Twelve patients improved and were discharged home while the remaining 10 discharged against medical advice. None of the patients received anti-retroviral drug treatment.

Table 3: Mean haematologic parameters of the patients

Parameter	Range	Mean (SD)
PCV (%)	10-40	24.8 (8.4)
WBC (cells/µL)	2600-26600	9961 (5774)
TLC (cells/µL)	928-9460	3932 (2880)
ESR (mm/hr)	38-72	60 (13)

Table 4: Causes of death among the patients

Diagnosis	No. of patients	No. of Mortalities	CFR (%)
Septicaemia	8	7	87.5
Tuberculosis	4	3	75.0
Pneumonia	3	1	33.3
*CSOM	7	0	0
Gastroenteritis	5	0	0

CSOM- Chronic suppurative otitis media

Discussion

The present study observed, *inter alia*, a predominance of oropharyngeal candidiasis as the opportunistic infection that commonly afflicts children with HIV infection in the community under review. This is essentially in keeping with reports from other parts of Nigeria such as the south-eastern region and the middle-belt area [14,15]. Similar observations had also been documented in many parts of Africa and other continents [10,12,16,17] culminating in the inclusion of oropharyngeal candidiasis among the illnesses used to define clinical paediatric HIV/AIDS by the WHO [13]. Childhood tuberculosis was the other OI observed among the patients in this study. This is not surprising as pulmonary TB remains an endemic disease in sub-Saharan Africa. Many researchers have directed attention to the impact of TB co-infection on paediatric HIV/AIDS [18-22]. This goes to show therefore that the battle against TB in Africa can only be won when the spread of HIV infection has been effectively curtailed. One major strategy that holds great promise in this regard is judicious use of highly active antiretroviral therapy (HAART) on affected patients as soon as indicated. Immune reconstitution has been reported to follow effective use of ARV therapy such that the incidence of OIs and other bacterial infections becomes substantially reduced in treated patients [23].

Another notable observation in the present study is the paucity of patients with pneumonia. Even though broncho-alveolar lavage was not done, none of the few patients that presented with pneumonia showed clinical or radiographic features suggestive of PCP. This is a major departure from previous reports that had identified PCP as a common OI associated with paediatric HIV/AIDS [8,9,11,24]. Whether or not this finding indicates that Pneumocystis carinii is not an endemic pathogen in our

environment remains to be seen and further research is required. Nonetheless, this observation tends to buttress the view expressed by some researchers that the patterns of opportunistic diseases are different in different parts of the world [25].

The finding of anaemia as a major co-morbidity among the subjects is in agreement with an earlier study from a sister hospital in the region [26]. Anaemia of chronic infection is a well-recognised entity in medical literature. Its pathogenesis stems from failure of iron release from its storage-site in the macrophages thereby making it unavailable for haemoglobin synthesis. Other contributory factors include reduced red blood cell survival and limited erythropoeitin response [27]. Furthermore the oropharyngeal inflammatory lesions and loss of appetite associated with HIV infection in many of the patients would have precluded adequate intake of haematopoeitic factors in the diet. Paediatric HIV / AIDS has been associated with a high mortality among African children affected by the disease. The present study observed a mortality rate of 33% amongst the subjects. This figure falls within the range of 26-59% reported for children aged 1-2 years by other workers [28]. It has also been noted that up to 75% of children with HIV infection in sub-Saharan Africa currently die before their fifth birthday [29]. This would explain why there was a very small number of patients aged above 5 years in the present study. One major reason for the high mortality of HIV infected children in sub-Saharan Africa is poor access to HAART, as evidenced by the fact that none of our patients had the benefit of antiretroviral therapy. It has also been observed that not more than 8% of HIV positive children needing treatment in low and middle income countries have access to antiretroviral drugs [30]. There is therefore a great need to commit more resources into the production of affordable and easy to use fixed-dose combination antiretroviral drugs in resource-poor countries in Africa and other parts of the world. Thus the on-going initiatives aimed at improving accessibility to anti-retroviral therapy in Nigeria being sponsored by the Federal Government and her partners are a step in the right direction.

Another aspect of paediatric HIV/AIDS management that needs to be strengthened in many countries with limited resources is capacity building in regard to laboratory support and services. We observed in our study that many important laboratory investigations both for diagnosis and monitoring could not be carried out largely due to lack of facilities and trained personnel. The most important among these tests include HIV RNA / DNA polymerase chain reaction assays, CD4+ cell count and viral load. Our experience also shows that the costs of these tests in the few places where they are presently available in our country are rather prohibitive and beyond reach for most of the patients that require them.

It is concluded that paediatric HIV infection in south-western Nigeria is most commonly associated with oral candidiasis, septicaemia and tuberculosis and a high mortality rate as a result of lack of access to ART.

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