Clinical predictors of HIV infection in hospitalized children aged 2 - 18 months in Harare, Zimbabwe

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Abstract

Background: In Africa without antiretroviral treatment more than half of the HIV infected children die by 2 years. The recommended HIV virological testing for early infant diagnosis is not widely available in developing countries therefore a presumptive diagnosis is made in infants presenting with symptoms suggestive of HIV disease.

Objectives: To identify presenting signs and symptoms predictive of HIV infection in hospitalized children aged between 2- 18 months at Harare Hospital, Zimbabwe.

Methods: In a cross sectional study the baseline clinical information was collected and HIV infection confirmed using DNA PCR. Multiple logistic regression analysis was used to identify significant predictors of symptomatic HIV infection. Diagnostic parameters (sensitivity, specificity) and their 95% confidence intervals were calculated.

Results: 355 children with an overall median age of 6 months (IQR: 3, 10.5 months) of whom 203 (57.2%) were HIV DNA PCR positive. Clinical signs independently predictive of HIV infection were cyanosis, generalized lymphadenopathy, oral thrush, weight for age z-score <-2 and splenomegaly. The sensitivity of these signs ranged from 43-49% with a higher specificity (ranging from 72.3-89.5%).

Conclusion: Clinical identification using individual signs for probable HIV infection in hospitalized children below 18 months would provide an opportunity for early diagnosis, treatment.

Key words: clinical predictors, HIV, hospitalized children

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Introduction

At present the greatest burden of HIV infections for both adults and children is known to be in the sub-Saharan Africa. It has been estimated that in 2009 up to 370,000 children below the age of 15 years were newly infected with HIV-1 and of these 260,000 had died[1]. Studies in Africa have documented that without antiretroviral treatment about a third of the perinatally infected children die by 1 year of age more than half die by 2 years[2].

Since transplacentally acquired maternal antibodies may persist up to 9- 12 months, HIV antibody test in an infant indicates exposure rather than confirmed infection[3]. A virological test(HIV nucleic acid test) HIV DNA polymerase chain reaction(PCR) can accurately identify HIV infection and will identify >95% of infants infected intrapartum and peripartum[4,5]. Although recently HIV virological testing using Dried Blood Spot has become more accessible in resource limited countries it is not yet widely available[5,6].

It is known that disease presentation of HIV infected children are non-specific and overlap with common childhood illnesses[7]. The limited availability of diagnostic facilities for virological testing underscore the need for identifying clinical predictors of HIV infection in the severely ill infants and children aged below 18 months. In 2006 World Health Organization (WHO) recommended clinical criteria for presumptive diagnosis of severe HIV disease in infants aged below 18 months requiring ART. This may still need to be used for identification of HIV infection among the ill and symptomatic children[8]. In 2008 WHO suggested that the use of presumptive clinical diagnosis in accordance with nationally defined algorithms would be required in settings with limited access to HIV virological testing[9].

The main objective of the study was to identify presenting signs and symptoms predictive of HIV infection in hospitalized children aged

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between 2- 18 months at Harare Hospital, Zimbabwe. World Health Organization (WHO)(2006) criteria for presumptive diagnosis of HIV-1 infection among symptomatic HIV-1 exposed children less than 18 months was also evaluated retrospectively in this study population[8].

Methods

A cross sectional study was conducted in the medical paediatric wards at Harare Central Hospital, which is a referral centre for Harare City Health clinics and health centers in the surrounding provinces. Ill children were either referred by the local clinics/ health centers or brought in by parents. The study population consisted of hospitalized children aged 2 to 18 months. Children presenting in moribund state requiring immediate resuscitation and if HIV status of the mother or the infant was already known, were excluded from the study. Children admitted from 8:00 to 12.00pm from Monday through Thursday were recruited for the study. During the study period HIV DNA PCR tests for infants were not routinely available at Harare Hospital.

Clinical assessments

A structured questionnaire was used to obtain relevant socio-demographic information and clinical history of children from the parent. Nutritional status was assessed using the weight for age measurement which was expressed as z-scores based on the WHO growth references[10]. A physical examination was conducted assessing for oral thrush, generalized lymphadenopathy, anaemia (clinical pallor),clubbing, duration of cough, pneumonia, diarrhoea, parotid swelling, discharging ears , dermatitis and other concurrent abnormal clinical findings using the WHO, Integrated Management of Childhood Illness(IMCI) guidelines definitions, where applicable[11,12]. A paediatrician conducted the clinical examination within 24 hours of admission and recorded his/her findings on a standardized form. Clinical records were reviewed for missing data and consistency within 24 hours.

Sample collection and Laboratory testing

After clinical assessment, blood sample was collected for HIV ELISA and DNA PCR. Plasma and cells were then obtained by centrifugation within 6 hours of blood collection and immediately stored at -80^0C until the assays were carried out. HIV antibody status of the infants was assessed using two locally approved kits: which consists of HIV 1.0.2 ICE; Murex Diagnostics, Edenvale, South Africa; and GeneScreen HIV1/2; Sanofi Diagnostics Pasteur, Johannesburg, South Africa. Duplicate pairs of discordant enzyme-linked immunosorbent assay test results were resolved by Western blot (HIV Blot 2.2; Genelabs Diagnostics SA, Geneva, Switzerland). HIV DNA PCR Roche amplification assay version 1.5(Roche Diagnostics, Branchburg, NJ, USA) was used as the reference standard for diagnosis of infant HIV-1 infection status. DNA extraction, amplification and detection were performed and results interpreted following the manufacturer's instructions as been previously described (13).

Sample size

We assumed that the clinical diagnostic test (such as the presence of oral thrush, generalized lymphadenopathy and severe malnutrition) had 90% sensitivity and 85% specificity using the HIV PCR DNA as the "gold standard." To achieve 95% confidence interval for the test sensitivity and specificity of 90% and 85% respectively, the sample size required was 196. An attrition rate of 50% was built into our sample size to allow for refusal by parents and the child being too sick giving a minimum sample size of 300.

Analysis

Demographic and clinical characteristics were summarized by HIV PCR DNA status. Significance testing of categorical variables was assessed using Chi-square test or Fisher's exact test and for the continuous variables student's t test or non-parametric equivalent were used. Multiple logistic regression analysis was used to identify significant demographic and clinical predictors of symptomatic HIV infection, Diagnostic parameters (sensitivity, specificity) and their 95% confidence intervals were calculated. The WHO(2006) recommended criteria for presumptive diagnosis for severe disease in children aged below 18 months was evaluated for its sensitivity, specificity and predictive values[8]. According to WHO recommendations, a presumptive diagnosis of severe HIV disease should be made if: the infant is confirmed as HIV antibody-positive and a diagnosis of AIDS indicator condition(s) can be made; or the infant is symptomatic with 2 or more of the following: oral thrush, severe pneumonia, severe sepsis[8].

Ethics Approval

The Medical Research Council of Zimbabwe and the Harare Central Hospital Ethics committee approved the study. Informed verbal consent was obtained from the mothers after appropriate explanation and reassurance regarding confidentiality of the test results. During the study period antiretroviral therapy was not available for the children below 2 years in Zimbabwe therefore they were put on cotrimoxazole prophylaxis only. The mothers were counseled and were referred to the adult HIV clinic for follow up and care, at Harare Hospital.

Results

Between July 2002 and May 2005, a total of 365 children aged 2 months to 18 months were enrolled in the study. All mothers were given pre-test and posttest counseling which included advising mothers and their partners to attend local VCT sites for HIV testing. Eight mothers (2.3%) refused tests on their children and two children with PCR indeterminate results were excluded from the analysis, leaving a total of 355. The male (192) to female ratio (157) was 1.2:1 and the median age was 6 months (IQR: 3, 10.5 months). Of the 215(60%) children who were found to be antibody positive, 12(5.6%) were found to be HIV DNA PCR negative, indicating HIV exposure but uninfected. Overall 203 (57.2%) of the children were found to be HIV-DNA-PCR positive. Table 1 shows the HIV infection status by age group. The highest infected group was aged 2 to 6 months.

Table 1: Baseline characteristics of the 355 children enrolled and their HIV status

	n(%)	Total
Gender: male	157(45.0)	349
WAZ<-2	154(47.8)	322
HIV antibody +ve	215(60.6)	355
HIV DNA PCR +ve	203(57.2)	355
2-6months(HIV+)	125(61.0)	205
7-11months(HIV+)	37(50.2)	74
13-18months(HIV+)	41(53.9)	6

Breastfeeding and immunization status

Three hundred and four (86.6%) children were still being breast fed at the time of the study. Their median age was 5 months (IQR 3,8months). Of the 47(13.4%) who had stopped breast-feeding the median age was 8 months (IQR 4,12 months). Child health cards were available for inspection for 85.6% children and appropriate immunization for age was found in 90%and 87% in the uninfected and HIV infected children respectively.

History of hospitalization

Overall 116(32.9%) mothers had reported their children having been hospitalized in the past. There was a statistically significant difference in the frequency of hospitalization among HIV infected, when compared to HIV un-infected children (39% VS 24.5%, p=0.004). There was no significant difference in the rate of past hospitalizations between HIV infected and uninfected infants in the age group 2 to 11 months but in the older age group past admissions were statistically significantly more frequent in the HIV infected group.

Table 2: Presenting complaints by the mothers on admission by infant HIV infection status

Presenting complaints	HIV –ve n/N (%)	HIV +ve n/N (%)	P-value
Fever	106/150(70.6)	146/202(72.3)	0.685
Cough	110/151(72.8)	162/202(80.2)	0.086
Difficulty in breathing	114/151(75.5)	155/201(77.1)	0.723
Diarrhoea	61/152(40.1)	65/202(32.2)	0.122
Persistent diarrhoea	3/152(2.0)	12/202(5.9)	0.068
Vomiting	60/151(39.5)	57/202(28.2)	0.023
Refusing feeds	82/149(55.0)	90/201(44.8)	0.047
Sores in mouth	26/147(17.7)	67/196(34.2)	0.001
Ear discharge	6/151(4.0)	23/202(11.4)	0.012
Rash	10/151(6.6)	7/202(3.5)	0.170
Parotid swelling	1/150(0.7)	8/196(4.1)	0.012
History of weight loss	30/138(21.7)	87/180(48.3	<0.001

The majority 54/116(46.6%) of the previous admissions were for pneumonia with similar proportions in both HIV infected and uninfected children. The second most frequent reason for admission was diarrhoea which was reported in total of 9 cases (7 in the HIV infected and 2 in the uninfected).

Nutritional status

Weights on admission were available in 322 (90.7%) of the children. The weight for age z-score (WAZ) of <-2 was documented in 154 (47.8% [42.2%,53.4%]) of the children. Amongst HIV infected children 110/183 (60.1%[52.7%,67.5%]) had WAZ<-2 compared with 44/139 (31.7%[26.3%,39.7%]) in the HIV uninfected group (P<0.001). Severe malnutrition, defined as WAZ below <-3 was present in 87(27.%[22%,32%]) in a significantly higher proportion 68(37.2%[29.9%,44.4%]) found in HIV infected children compared to 19(13.7%[7.6%,19.7%]) in the uninfected (p<0.001).

Treatment for tuberculosis (TB) among parents

Of the 338(95.2%) mothers who responded to the question about TB infection among the parents of the children, 28(8.3%) gave a positive history of past or ongoing TB treatment among parents. About 12% of the HIV infected children (23/195) and 3.5% of the uninfected children (5/143) had parents with history of having been or being treated for TB (p=0.006). During hospitalization 3.1% (6/195) of the HIV infected children were treated for tuberculosis and none in the HIV uninfected group.

Presenting complaints

The frequency of presenting complaints of fever, cough, difficulty in breathing, diarrhoea and rash were similar in both HIV infected and uninfected children except, refusing feeds (p=.047). However, oral sores, ear discharge, parotid swelling and history of weight loss as perceived by the mother were found to be significantly more common among the HIV infected children compared to the uninfected. When stratified by age, sores in the mouth was significantly higher in the HIV infected group only among 2 to 11months age group whilst parotid swelling was found to be significantly higher in the group 12 to 18 months HIV infected children.

A total 107/318(36.8%) of the mothers reported weight loss in their children, 48.3% in the HIV infected and 21.7% in the HIV uninfected (p<0.001). The overall sensitivity and specificity of the maternal perception of weight loss compared with weight for age z-score <-2 was 70% and 80% respectively (Positive predictive value = 72% and Negative predictive value = 82%).

Multivariate analysis of the presenting complaints including a history of treatment for TB infection among parents (table 3) showed that infants with either parent, who had history of being on treatment for tuberculosis or presently on TB treatment, history of weight loss, presence of rash and parotid swelling, were found to be independent predictors of HIV infection. Within each age group weight loss, as observed by the mothers, remained an independent predictor of HIV infection. Among the age group 12 – 18 months presence of ear discharge was also an independent predictor of HIV infection.

Table 3: Multivariate analysis of the presenting complaints including history of treatment for TB infection among parents

Presenting features	Adjusted Odds ratio	95% CI
Parent TB	3.81	(1.3, 11.1)
Diarrhoea	1.8	(1.0, 2.80)
Vomiting	1.8	(1.0. 3.10)
Rash	4.5	(1.1,16.7)
Ear discharge	2.71	(0.81, 9.0)
Parotid swelling	13.8	(1.04, 180.84)*
Weight loss	3.68	(2.1, 6.5)

* indicates wide CI

Clinical features

Comparison of the clinical features by univariate analyses showed that pallor, cyanosis, pneumonia, generalized lymphadenopathy, parotid swelling, oral thrush, ear discharge, hepatomegaly and splenomegaly were statistically significantly more common in the HIV infected compared to uninfected children (table 4).

Table 4: Clinical features among HIV infected and uninfected

Clinical features	*HIV -ve n/N(%)*	*HIV +ve n/N(%)*	*p value*
Pallor	42/152[27.6]	85/202[42.0]	0.005
Cyanosis	34/151[23.0]	88/202[43.6]	<0.001
Pneumonia	106/151[70.0]	162/201[80.0]	0.023
Jaundice	4/149[2.6]	1/199[0.5]	0.093
Oedema	16/140[3.6]	12/185[6.5]	0.211
Gen lymph	21/152 [13.8]	91/202[45.0]	<0.001
Clubbing	5/148 [3.4]	12/199[12]	0.258
Rash	23/149[15.4]	46/201[22.3]	0.830
Parotid swelling	1/151[0.7]	16/202[7.9]	0.002
Oral thrush	15/151[9.9]	99/202[49.0]	<0.001
Ear discharge	2/151[1.3]	17/203[8.4]	0.004
Hepatomegaly	42/151[27.8]	131/203[64.5]	<0.001
Splenomegaly	10/151[6.6]	85/203[41.9]	<0.001

On multivariate analyses only cyanosis (indicating very severe pneumonia), generalized lymphadenopathy, oral thrush, bilateral parotid swelling, WAZ<-2 and splenomegaly remained independent associated with HIV infection after controlling for other variables (table 5).

Table 5: Multivariate analysis of clinical features for identifying independent predictors of HIV infection

Clinical features	Adjusted odds ratio	95% CI
Cyanosis	3.01	(1.6, 5.7)
Generalized lymphadenopathy	2.13	(1.1, 4,3)
Oral thrush	8. 30	(3.8, 18.3)
Parotid swelling	10.78	(1.2, 100.1)*
WAZ <-2^	3.87	(2.0, 7.4)
Splenomegaly	9.2	(4.0,21.0)

* indicates wide CI, ^weight for age z-score

The identified individual clinical predictors of HIV infection were further evaluated for sensitivity, specificity and positive and negative predictive values (table 6). Overall a high specificity ranging from (78.4-90.1%) was recorded with positive predictive values and negative predictive values being (72.3-89.5%) and (53.5-45%) respectively. Oral thrush, weight loss, WAZ<-2 and generalized lymphadenopathy were each found to have sensitivity of 45% and above.

Evaluation of the WHO presumptive diagnosis of severe HIV disease in infants

The common AIDS defining illness in young infants is PCP pneumonia which was not confirmed in this study. Other AIDS indicator conditions such as cryptococcal meningitis, HIV wasting, Kaposi sarcoma, extrapulmonary TB was not found in this age group[8]. Since sepsis was an uncommon diagnosis in this setting (2%), only oral thrush and severe pneumonia were evaluated for sensitivity, specificity and predictive values against positive HIV DNA PCR.

It was found that an HIV antibody positive infant with severe pneumonia and oral thrush had a sensitivity of 36.6% (CI: 30.0, 43.3) specificity 98.7% (CI: 96.9,100.0) with a positive predictive value 97.4%, and negative predictive value of 54.1%. Infants with severe pneumonia and oral thrush, without taking into positive HIV antibody into consideration, had sensitivity of 37.6% (CI:30.9, 44.3) specificity 92.2%(CI:87.9,96.4) with a positive predictive value of 86.5%, negative predictive value of 52.5%

Common diagnoses and mortality

Severe/very severe pneumonia and diarrhoea were the most frequently diagnosed conditions among these infants. Overall 76% were diagnosed with pneumonia, 80% in the HIV infected and 70% in the HIV uninfected (p=0.023) group. Thirty six percent had diarrhoea with or without pneumonia and of these 15/126(12%) had persistent diarrhoea. There was no significant difference in the proportion of children with diarrhoea between the two groups.

During hospitalization a total of 75/ 344(21.8%) infants died with the majority of the deaths occurring among 61/195(31.3%) HIV infected versus 14/ 149(9.4%) among the HIV uninfected (p<0.001).

Table 6: Sensitivity, specificity and predictive values of the independent predictors of HIV infection

	Sensitivity (%)	*Specificity (%)*	*PPV (%)*	*NPV (%)*
Parent TB	11.9(7.3,16.4)	96.5(93.5,99.5)	82.0%	45%
Weight loss	48.6(41.3, 55.9)	78.4(71.6,85.3)	75.1%	53.3%
Cyanosis	43.8(36.9,50.6)	77.6(71.0,84.3)	72.3%	50.8%
Oral thrush	49.3(42.3,56.2)	90.1(85.4,94.9)	87.0%	57.1%
WAZ <-2^	47.6(40.4, 54,8)	76.6(69.6,83.6)	73.1%	52.2%
Splenomegaly	42.1(35.5,48.9)	93.4(89.5,97.4)	89.5%	54.7%
Gen lymph	45.0(38.2,51.9)	84.6(79.0, 90.0)	79.6%	53.5%
Parotid swelling	8.0(4.2,11.7)	99.3(98.1,100.6)	94.2%	44.7%

PPV= positive predictive value, NPV=negative predictive value,^weight for age z-score

Discussion

This study describes clinical signs and symptoms which would assist in predicting HIV infection in hospitalized infants and children aged 2- 18 months in health institutions, where HIV-DNA-PCR for confirmation of infection in HIV-exposed infants may not be easily accessible. In developing countries, including Zimbabwe, often the first opportunity for identifying HIV infection in an infant or a child presents during hospitalization or when attending health centers. Due to various reasons, a proportion of pregnant women do not access antenatal care in Zimbabwe, missing the opportunities for HIV testing and prevention of transmission to infants provided by Prevention of Mother to Child Transmission (PMTCT) interventions[13].

The prevalence of HIV infection in this study population was 57%. Severe pneumonia/very severe pneumonia, diarrhoea and malnutrition were most common reasons for hospitalization for both HIV and uninfected children. These three conditions remain predominant causes of morbidity and mortality among children in developing countries including Zimbabwe[15,16]. Morbidity is known to be higher and more severe among the HIV infected than uninfected children in Africa[17,18]. A higher proportion of HIV infected children aged 12-18 months had been previously hospitalized, compared to the uninfected. Among the younger infants there were no differences in the frequency of past hospitalizations between the HIV infected and uninfected. Among infants aged below 6 months, admission during the study was the first hospitalization for 75% of infants (70%HIV infected, (80%) HIV uninfected). Therefore the first serious illness in an HIV exposed young infant below 6 months is likely to be manifestation of severe symptomatic HIV disease.

Significantly higher proportion of HIV infected children were underweight or severely malnourished than the HIV uninfected. Malnutrition and failure to thrive is a common early feature of untreated HIV infected infants and children[19, 20, 21]. Of importance was that the overall mothers' perception of weight loss was highly predictive of WAZ less <-2 at presentation. Both mothers' perception of weight loss and the WAZ<-2 on admission were independently predictive of HIV infection. In our setting, the mother's perception regarding weight loss should be regarded as an important possible indicator of HIV infection in the ill child.

A parent who had been or presently on TB treatment was found to be associated with HIV infection in the child in this study setting. HIV exposed and HIV infected children are at greater risk of Mycobacterium tuberculosis from HIV infected parents who may be co-infected TB[22]. TB and HIV co-infections are common, and an estimated 70% of TB cases are co-infected with HIV in Zimbabwe[23]. Since the diagnosis of tuberculosis in children is often based on clinical and radiological criteria only, it is likely to be missed or underestimated even in referral institutions[24].

Although cyanosis, pneumonia, generalized lymphadenopathy, parotid swelling, oral thrush, ear discharge, hepatomegaly and splenomegaly were

present in both HIV infected and uninfected children they were statistically significantly more common in the HIV infected children. Similar findings were observed in a Ugandan study of hospitalized children aged below 18 months[25]. This highlights the overlap of symptoms and signs between HIV infected and uninfected children below 18 months of age[7].

We found clinical signs independently predictive of HIV infection to be cyanosis (indicating very severe pneumonia) generalized lymphadenopathy, oral thrush, parotid swelling, WAZ<-2 and splenomegaly. The sensitivity of each of these signs was low, ranging from 43-49% indicating some limitation of its use in the diagnosis of HIV infection in children who are severely ill. However, a higher specificity (ranging from 72.3-89.5%) was recorded indicating that lack of these symptoms is helpful in predicting absence of HIV disease therefore would reduce the risk of over diagnosing HIV infection. These individual clinical signs would be useful in identifying probable HIV infection in these severely ill children whilst awaiting a confirmatory HIV-DNA-PCR test.

Few studies have evaluated WHO clinical criteria for presumptive diagnosis of HIV infection among severely ill infants below 18 months. A low sensitivity of 43% and a high specificity of 88% was recorded for the WHO algorithm (without CD4%) when used for the diagnosis of HIV-1 infection among HIV exposed children less than 18 months identified from general paediatric wards and the outpatients clinics in Nairobi, Kenya[26]. The positive predictive value was 54%, suggesting a lower prevalence of severe HIV disease among the study population, which also included the less ill children from outpatient clinics.

A validation of WHO Presumptive diagnosis of HIV-1 infection among HIV exposed hospitalized children less than 18 months, was recently undertaken in Rwanda. HIV infection was confirmed using DNA-PCR in 53% of the 236 HIV exposed children, which formed their study population. The criteria used for evaluation consisted of severe pneumonia, oral thrush, septicaemia and inclusion of "severe unexplained malnutrition" (weight for age <-3sd), which is a stage 4-defining criterion. A sensitivity of 76.6% and a specificity of 52.7% (PPV=64%, NPV=67%.was found[27]. The high sensitivity in this study was explained by the contribution of inclusion of "severe unexplained malnutrition", which was documented in 52% of their study population. In comparison, a lower frequency of 27% were severely malnourished (37% and 14% of HIV infected and uninfected children respectively) in our study population.

Presumptive diagnosis of severe HIV disease using severe pneumonia with oral thrush in the presence of a positive HIV antibody test was evaluated in this study. A high positive predictive value of 97.4 %(with low sensitivity of 36.6% and a high specificity of 98.7%) was noted. When only 2 conditions, severe pneumonia and oral thrush were assessed the positive predictive value still remained above 85% (sensitivity of 37.6% and specificity of 92, 2%). It appears that in our hospitalized study population the combination of severe pneumonia and oral thrush would be useful for the clinical identification of probable HIV infection

These young symptomatic HIV infected children most likely represent the rapid progressors who may have acquired the infection in utero or during early post-natal period and are associated with high viral load and low CD4%[28].This group is at high risk of severe opportunistic infections especially *Pneumocystis jiroveci* which is known to be the most common cause of severe pneumonia contributing to both high morbidity and mortality [29-31].

The generalizibility of the study findings is limited to a hospital setting where critically ill infants and children are referred for care and of concern is the low sensitivity of the clinical criteria, in this setting. The inclusion of CD4 assays would have been useful and may have strengthened this study. However the number of children with a positive antibody test with a negative HIV DNA PCR was less than 6% indicating that HIV antibody test in young hospitalized children would be useful for the diagnosis of HIV in the majority of cases.

Early identification of HIV infected infants before development of symptoms and followed by appropriate management, would improve survival[32,33]. A feasible and acceptable strategy would be the use of health facility contacts through child growth monitoring and immunization visits, which provides multiple opportunities for HIV testing in both asymptomatic and symptomatic infants and children[34]. The need for reliable, cheap and easily accessible diagnostic tests for infants with HIV-1 including PCR cannot be over emphasized.

Conclusion

This study has identified clinical signs among hospitalized infants and children which are independently predictive of HIV infection, but with

low sensitivity in our high HIV prevalent referral setting. These clinical findings suggestive of severe HIV disease can be identified in resource limited setting since they also constitute symptom based algorithm for the diagnosis of HIV in older children as part of IMCI strategy[35]. The very high mortality recorded among the HIV infected underscores the need for an effective and aggressive PMTCT programme, with special emphasis on early identification and appropriate care and treatment of the HIV infected infants and children.

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