

**IMPACT OF HIV ON CHILDHOOD
MORBIDITY AND MORTALITY AMONG
UNDERFIVE CHILDREN HOSPITALISED
AT THE UNIVERSITY TEACHING
HOSPITAL (UTH), LUSAKA.**

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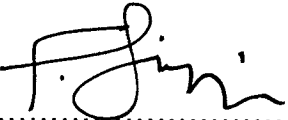
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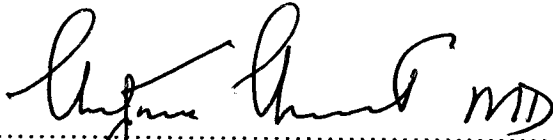
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DECLARATION

I hereby declare that this dissertation represents my own work and has not been presented either wholly or in part for a degree at the University of Zambia or any other University.

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APPROVAL

This dissertation of Dr. Fredrick Sinyinza is approved as fulfilling the requirement for the award of the degree of Masters of Medicine in Paediatrics and Child Health by the University of Zambia.

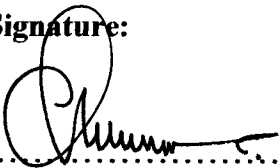
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ABSTRACT

Zambia is among countries in the Sub-Saharan African with high HIV seroprevalence Rates. In spite an increased awareness campaign concerning the dangers of HIV/AIDS and its prevention, the infection has continued to spread. The current impact of the HIV infection on childhood morbidity and mortality is not well known, particularly in developing countries. The mode of transmission in the adult population of the Sub-Saharan region is mainly heterosexual. The commonest mode of transmission in children is by vertical transmission.

The main objective of the study therefore was to look at the impact of HIV on childhood morbidity and mortality among under five children hospitalized at the University Teaching Hospital children's wing. The study was conducted in 1999 between August and October. This was a descriptive cross sectional study involving children aged between two months and five years admitted to the hospital during this period. parents/guardians of children in the study were interviewed and HIV voluntary counseling and testing services were provided. Only those children whose parents consented to a blood test for the presence of HIV antibodies were enrolled on to the study .The information obtained was recorded by using a standard questionnaire. The study revealed that most of parents were willing to know the HIV serostatus of their children as demonstrated by the 83% acceptance rate. The seroprevalence rate was 40% for children aged above 18months (confirmed infection), and 38% for those aged below 18 months (suspected infection). The Maternal blood was not tested for HIV

antibodies due to financial constraints. The magnitude of HIV infection in non-Hospitalised children still remains unknown. The leading causes of admission in HIV positive children were Protein Energy Malnutrition, Tuberculosis, Pneumonia and Diarrhea Diseases. These diseases were also the common causes of admissions in HIV negative children although the morbidity was higher in the former. The common causes of death in HIV positive children were PEM, Pneumonia, and Diarrhoea Disease.

Although they were also among the common causes of death in HIV negative children, the mortality rate was much higher in HIV positive children. The overall mortality rates were 22% for HIV positive children and 14% for HIV negative children. The study has also reviewed that most of the HIV positive children had a history of having lost a sibling in their family, probably due to HIV related morbidity.

In conclusion, in order to reduce the impact of HIV infection on childhood morbidity and mortality, there is need to step up more aggressive interventions so that mother to child transmission of HIV can be greatly reduced. At the time of the study the overall HIV seroprevalence rate in the community was 19.7 %.

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F. Sinyinza

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GLOSSARY

ADD	-	Acute Diarrhoea Disease
AIDS	-	Acquired Immuno Deficiency Syndrome
ART	-	Anti Retroviral Therapy
AZT	-	Azido Thymidine
BCG	-	Bacille Calmette Guerin
CMV	-	Cytomegalo Virus
DNA	-	Deoxyribo Nucleic Acid
ELISA	-	Enzyme Linked Immunosorbent Assay
PCP	-	Pneumo Cystis Carinii
PCR	-	Polymerase Chain Reaction
PEM	-	Protein Energy Malnutrition
TB	-	Tuberculosis
UN	-	United Nations
UTH	-	University Teaching Hospital
VCT	-	Voluntary Counseling and Testing
WHO	-	World Health Organisation

CHAPTER 1

1.0. INTRODUCTION

1.1.0. Background

The first recognised cases of the Acquired Immuno-deficiency Syndrome (AIDS) occurred in the summer of 1981 in America. Even though the condition became known early as AIDS, its cause and mode of transmission were not immediately obvious. The virus that causes AIDS was discovered in 1983, and given various names (1). The internationally accepted term is now the Human Immunodeficiency Virus (HIV). Subsequently a new variant was discovered in 1986 in patients with West Africans connections - HIV-2 (2). The Joint United Nations Programme on AIDS (UNAIDS) and World Health Organisation (WHO), estimated that by the end of the year 2000 there were 36.1 million people living with HIV/AIDS worldwide, from which 34.7 million were adults and 1.4 million were children aged below 15 years. During the same year there were 5.3 million new HIV infections with approximately 16000 new infections per day. During the same year a cumulative 21.8 million people were estimated to have died from HIV/AIDS associated illness, among them about 600000 children. Death due to HIV/AIDS alone was estimated at three million. In addition this pandemic has created a cumulative total of 13.2million orphans (3).

Over 90% of people living with HIV worldwide reside in developing countries. Sub-Saharan Africa is the region worst affected with about 70% of the worldwide infection. Most of these infected people will die in the next 10 years, adding to the 13.7 million Africans already claimed by the epidemic. About 80% of deaths in the year 2000 occurred in Africa. The predominant HIV transmission in this part of Africa is heterosexual. This mode of transmission is responsible for most of the 3.4 million new HIV infections each year in this region. High fertility rates combined with poor access to information and services for prevention of mother to child

transmission have resulted in 500000 infants being infected perinatally each year. Southern Africa now estimates that 2.4 million people are living with HIV. In Botswana the number of adults infected has doubled over the last five years now reaching 25-30% of the adult population. In Zimbabwe infection is estimated at 20%. In these severely affected countries, this epidemic has wiped out most developmental gains (4).

Although HIV was introduced later in Asia, the epidemic is escalating rapidly in this most populous region of the world. Currently an estimated six million people are infected, the largest number of which are in India. The Americas represent the region with the third largest number of HIV infection, at 2.4 million infected individuals. In the Western and Eastern Europe, 700,000 adults and children are living with HIV/AIDS (4).

1.1.1 Zambia

The first case of AIDS was reported in Zambia in 1984 in response to this the government established the National AIDS Surveillance and the Inter-sectoral AIDS Health Education committees in 1986 (5). Prior to the emergence of HIV/AIDS epidemic in Zambia, Blood transfusion was hospital based with no standard National Donor Selection criteria and no legislation to govern the practice. In response to this, in 1988 the Global Safety Initiative was launched by the WHO to set up universally applicable standard for collection, processing and use of blood. This programme was sponsored by the European Union through the multilateral agreement. In 1988 all District hospitals started screening blood for HIV (6).

According to the 1998 estimations from the Ministry of Health / Central Board of Health, 19.7% of the entire adult population aged between 15 and 49 years were already infected, representing an absolute number of 1.09 million Zambians infected, among which 923000 were adult and 87000 children. Almost all of these will develop AIDS and die within the next 10 years or so. In urban areas the prevalence rates among 15 to 49 years old were more than 28% and that of

Trends in Early Childhood Mortality Rates Since 1977.

Period	Infant Mortality Rate	Under 5 Mortality Rate
1977 - 81	97	152
1987 - 91	107	191
1992 - 96	109	197
1998 - 2001	95	168

A comparison of the mortality rates found in the 2000 Zambia Demographic Health Survey (ZDHS) with the rates from two earlier DHS suggests that mortality among young children has declined from the fairly stable levels observed in the late 1980s to mid–1990s. However, more detailed analysis of the mortality data from all three surveys is needed to confirm the nature and magnitude of the trend in early childhood mortality over the past two decades in Zambia (10,11).

A lot has been done in Zambia concerning the prevention of HIV transmission. Both the government and the Non- Governmental Organizations (NGOs) involved in HIV/AIDS programmes recognise the importance of a continuum of care. This includes efforts to prevent HIV infection in the first place, provision of voluntary counselling and spiritual and emotional support, provision of medical care to persons infected or who are living with AIDS and also provision of support for persons affected by the epidemic (widows and orphans). In order to reduce the incidence of paediatric new infections various approaches are being used in Zambia. Some of these approaches are as follows:

- (1) Provision of voluntary counselling and testing (VCT) and access to family planning services.
- (2) Reduction of HIV transmission during breast-feeding: –About 30% of maternal to child

transmission (MTCT) occurs through this route. Curtailing breast-feeding or reducing the time an infant is exposed to infected breast milk could reduce transmission of HIV but would eliminate the significant health benefits that children get from breast-feeding. For this reason, international guidelines have tended to recommend continued breast-feeding especially during the early months following birth. In some cases mothers could be counselled on alternative ways to feed their child if they so choose and can afford.

- (3) Using Anti retroviral Drugs – MTCT can be reduced through the use of short duration of anti-retroviral drugs such as Zidovudine and Nevirapine in Zambia.

1.2.0. Literature Review

The Acquired immuno-deficiency syndrome (AIDS) was first reported in children in 1983. This is caused by a virus (HIV) belonging to a group of the lentiviruses of the sub-family retroviridae. There are two types of HIV, namely HIV-1 and HIV-2. The later is currently restricted to West Africa and countries with historical or commercial ties to this region. HIV1 is found throughout the world and is responsible for the majority of the cases. HIV-1 strains are further classified into group M (major) and group O (outlier) strains. Group M viruses are a prevalent group accounting for the majority of the HIV infections throughout the world .The group O strains are rare and are quite diverse from the group M viruses. There is a further subdivision of HIV-1 viruses into sub-type and these bear the letters of the alphabet from A to J. The commonest HIV-1 in the Southern part of Africa sub-type C. HIV-2 possesses five sub-types. The reason for the genetic diversity of the viruses is related to the inherent potential of the virus to mutate and in some instances is due to recombination of distinct virus strains. The implication of the genetic diversity of these viruses relate to viral diagnostics, vaccine development and possibly to differing rates of clinical progression of the HIV infection (12).

Each HIV particle is composed of two copies of the single-stranded RNA viral genome packaged inside a protein core or cap. The core (Gag) protein includes the major structural proteins p24 (capsid) and p17 (matrix), the internal structure protein p7 (nucleocapsid) and the Gag-pol precursor protein p55. The virus particle also contains polymerase (pol) proteins that are essential for the early steps in the life cycle of the virus. These are the reverse transcriptase p66/p51 and the endonuclease p31. The capsid of the HIV is surrounded by a lipid envelope derived from the infected cells in which HIV envelope glycoproteins (Env) are embedded. These include the outer envelope glycoprotein gp120, the transmembrane glycoprotein gp41 and the precursor glycoprotein gp160 (13).

1.2.1. Mode of Transmission of HIV Infection in Children.

The mode of transmission in the adult population of the Sub-Saharan region is mainly heterosexual. The commonest mode of transmission in children is by vertical transmission. This occurs either during pregnancy, during labour and delivery (75%) or through breast-feeding (30-45%). Evidence from prospective cohort studies shows that the risk of HIV transmission from mother to child is increased by either recent primary infection or advanced HIV disease in the mother or prematurity in the baby. Moreover, factors around delivery also play a role, including prolonged rupture of membrane. Mother to child transmission (MTCT) alone accounts for about 90% of childhood HIV infection. Other modes of HIV transmission in children can be due to blood transfusion, unsterilised procedures /injuries or due to sexual abuse (14,15,16).

1.2.2. Pathogenesis of HIV Infection.

HIV infects certain types of cells, usually cells that express CD4 receptors. Such cells include T-helper cells (or CD4 cells) Monocytes and Macrophages. Other types of cells that express CD4 receptors, that can therefore be infected with HIV include Glial cells in the central nervous

system, Chromaffin cells in the intestines and Langerhans cells in the mucous membrane and the skin. Certain human cells surface proteins in addition to CD4 have been found to be crucial for HIV-1 entry. These are known as co-receptors. Two co-receptors for HIV believed to mediate fusion between HIV and its target cells have been identified. These are C-C chemokine receptor CCR-5 expressed by Monocytes and Lymphocytes, and C-X-C Chemokine receptor CXCR-4 (also known as Fusin) expressed on T-Lymphocytes. This explains why Monocytotropic strains of HIV can infect both monocytes and primary lymphocytes (both of which express CCR-5), but not T-cell lines (which lack CCR-5), and why T-cell tropic strains of HIV-1 cannot infect monocytes (which lack CXCR-4). The CCR-5 and CXCR-4 co-receptors normally function as receptors for chemo-attractant cytokines (chemokines) in the body. These chemokines are produced by CD8 T-cells in response to immune activation (17,18).

1.2.3. Natural Resistance.

Some individuals appear to remain uninfected by HIV despite repeated exposure to the virus. This observation might be attributed to the responses by the co-receptors, cytotoxic T-lymphocyte, or due to some other mechanisms yet to be identified. Certain forms mutations in the chemokine co-receptor molecule confirm resistance to HIV infection. Individuals who are homozygous for the CCR-5 deletion do not express CCR-5 and their peripheral blood mononuclear cells are resistant to infection with monocytotropic HIV-1. Individuals with this deletion appear to be resistant to HIV infection. It has also been suggested that individuals who are heterozygous for their CCR-5 deletion may have a slower rate of disease progression than those who are homozygous for the wild type allele, although this appears to be limited to those infected with monocytotropic HIV strains. It is important to remember that almost all sexual infections results from monocytotropic chemokine receptors, strains. Polymorphism in genes of

other including CCR-2, the promoter region of CCR-5, and the stromal –derived factor (natural ligand for CXCR-4R), have been shown to influence the pathogenesis of HIV disease (19).

1.2.4. Forms Of Progression Of Infection

Paediatric HIV infection progress more rapidly than that of adults. There are three distinct patterns of the HIV disease in children, which have been described, and this are as follows (20):

- (1). Rapidly progressive form: - Characterised by rapid progression of the disease within a few months after birth probably due to immature immune response. Onset of AIDS usually occurs within the first few months of life. If untreated median survival age is between 6 to 9 months. In most of these children the virus can be detected by PCR within the first 48 hours. The infection is believed to occur in utero.
- (2). Slow progressive form: - The majority (75%) of the infected children are found in this group. It is postulated that infants get infected during the intrapartum period. HIV cultures are usually negative in the first week of life, and median survival age is 6years.
- (4) Long term survivors: - these children get infected during perinatal period. They have minimum or no progression of the disease with relatively normal CD4 count and very low viral load for more than 8years.

The progression of the HIV infection will partly depend on the factors mentioned above.

1.2.5. Diagnosis Of HIV Infection In Children.

HIV infections in infants are diagnosed mainly on the basis of clinical signs, in a child with HIV antibodies. In developing countries, clinical diagnosis and the presence of HIV antibodies may be used in making the diagnosis of HIV infection. This is so because better laboratory tests like PCR, Antigen tests and viral cultures are too expensive or simply not available. HIV antibody tests do not give a true picture of the child's HIV status before the age of 18 months due to the presence of maternal antibodies (21,22). Early serologic diagnosis may be made by detection of

the presence of Immuno-globulins M antibodies or particularly of specific immuno-globulin A by ELISA. This has been shown to be reasonably conclusive in ages between 1-6 months, but their low sensitivity in the first weeks of life following peri-natal infection, still further limits their usefulness. In the developed world, it has been accepted that detection of the virus by molecular DNA techniques now offers a highly accurate diagnostic method in any baby aged 2-3 months (23). However such sophisticated techniques are too expensive for economically challenged countries. For countries with limited laboratory diagnostic techniques WHO has developed a paediatric HIV clinical diagnostic criteria, as shown below. According to these WHO criteria the case definition of paediatric AIDS is fulfilled in the presence of at least 2 of the following major signs and 2 minor signs, in the absence of a known cause of immune suppression (24).

The major signs/symptoms are:

- (1) Weight loss or abnormally slow growth
- (2) Chronic diarrhoea (> 1 month)
- (3) Prolonged fever (> 1 month)

The minor signs/symptoms are:

- (1) Generalised lymphadenopathy
- (2) Oro-pharyngeal candidiasis
- (3) Persistent cough
- (4) Recurrent common infection, for example pharyngitis ear infection.
- (5) Generalised rash

Confirmed HIV infection in the mother is considered as minor criteria.

The diagnosis of HIV/AIDS in children in Zambia is mainly clinical, and may be confirmed by HIV antibody testing, where available. In 1992 clinical diagnostic criteria were developed to suit the Zambia situation. This was developed by modifying the W.H.O criteria. Studies done

revealed that this modified type was more sensitive and specific (25). The Zambian diagnostic criteria is as shown below;

Major signs: (1) Recurrent fever of at least a month's duration.

(2) Recurrent oral pharyngeal candidiasis.

(3) Recurrent respiratory infections.

Minor signs: (1) chronic diarrhoea of at least one month's duration.

(2) Weight loss or abnormally slow growth.

(3) Generalised lymphadenopathy.

(4) Persistent cough of at least one month's duration.

(5) Extra-pulmonary tuberculosis.

(6) Pneumocystis carinii.

(7) Confirmed maternal HIV infection.

Paediatric AIDS is suspected in a child less than 14 years of age presenting with at least 2 major and 2 minor signs in the absence of known causes of immuno-deficiency.

1.2.6. Opportunistic Infections.

- (1). Pneumocystis Carinii Infection (PCP): Pneumocystis carinii pneumonia has a peak incidence of 3 –6 months. It is the most common AIDS defining condition in children. Infants commonly present with tachypnoea, dyspnoea, and progressive hypoxia (26). This infection is treated with high doses of Co-trimoxazole and prednisolone for at least 21 days, pentamidine and Dapsone has also been used as an alternative drugs.
- (2). Oro-pharyngeal candidiasis: In children infection may spread to the oesophagus. It usually responds well to anti-fungal drugs such as Ketoconazole and fluconazole but has a tendency to recur.
- (3). Cytomegalovirus (CMV) Infections: This infection is difficult to diagnose because

CMV may be present without causing an overt disease. Respiratory signs may not be marked and the chest x-rays may show nothing. It may occur in association with PCP in babies in the first months of life.

- (4). Cryptosporidiosis: The infection usually involves children between three and four years of age. It causes chronic, painful profusely watery diarrhoea leading to weight loss. This infection is also associated with high mortality rate.
- (5). Other Opportunistic Infections: Numerous other organisms may cause serious infections. These patients are prone to developing recurrent serious bacterial infections. Tuberculosis, which is at present on the increase, is a threat to children. Other opportunistic infections, which are increasing with the advent of HIV infections, are toxoplasmosis and cryptococcal infections.

1.2.7. Management Of HIV Infection in Children

General management of HIV infected children includes good nutrition, vaccinations against common childhood diseases and treatment of opportunistic infections (27). In richer countries HIV infected children are treated with Anti Retroviral therapy (ART). These drugs have been shown to markedly improve the quality of life, reduce the viral load, increase CD4 count and reduce the frequency of hospital admissions. However, they are very expensive for developing countries. Patients on these drugs also need to be carefully monitored for adverse effects. The response of infected children to ART is good and there are paediatric preparations for some of the drugs currently licensed for use in adults (28,29).

1.2.8. Prevention Of HIV infection In Children.

The most effective way of preventing HIV infections in children is to prevent infection in the mother. Prevention of MTCT can be achieved by the use of anti-retro viral drugs. The administration of Zidovudine (AZT) alone or with 3TC and Nevirapine during pregnancy,

childbirth and after birth is now being heavily promoted (30). In developing countries short regimens are being employed. About 15% of children born from HIV positive mothers get infected through breast-feeding. However, for women who are HIV positive and do not have any access to appropriate alternatives breast-feeding is still recommended (31). Studies have shown that use of cotrimoxazole prophylaxis in HIV infected adults has resulted in reduced mortality rate due to opportunistic infections; however, this has not yet been proven in children in developing countries.

CHAPTER 2.

2.0. OBJECTIVES OF THE STUDY.

2.1. Main Objective.

To determine the impact of HIV/AIDS on childhood morbidity and mortality among under-five children hospitalised at UTH.

2.3. Specific Objectives.

1. To determine the pattern of clinical disease between HIV infected and non-HIV infected hospitalised children under five years of age.
2. To compare the hospital mortality rates, in probable HIV infected (<18 months), infected (>18 months) and uninfected children.
3. To compare the social family circumstances of HIV positive children with that HIV negative children.

CHAPTER 3

3.0. METHODOLOGY

3.1. Study Design

This was a descriptive cross sectional (prevalence) study involving children aged below five old admitted to the children's wing of the University Teaching Hospital (UTH).

3.2. Study Site.

This study was undertaken in the Department of Paediatrics, UTH. This is the biggest hospital in Zambia, and also the only public hospital in Lusaka. It serves as a national tertiary referral centre as well as a referral centre for Lusaka Province. The hospital also provides health services for un-referred patients. The children's wing has a bed capacity of 364, and it admits about 2000 sick children every month. The Paediatrics Department has five units, namely units one up to four and has a Neonatology unit. Each unit is headed by a consultant and are all involved in the management of general paediatric patients, except unit IV the neonatology unit. Unit IV is a Nutrition unit. The other units (I, II, and III) manage general paediatric cases and minor sub-specialities. Each of these first four units admits patients every fourth day. On first presentation patients are seen in the outpatient filter wing of the hospital. Those requiring hospital care admitted in the admission ward for at least a day before being transferred to their respective wards, depending on the unit admitting that day. Children with severe malnutrition go to the malnutrition ward straight, they do not the admission ward. These are admitted directly from the outpatient wing to their respective wards.

3.3. Study Population.

This study included children aged between 2 months and 5 years who were admitted to children's wards via the outpatient wing. Children were recruited during a period between August and October 1999. After admission they were reviewed daily in their respective wards

until either discharge or death.

The criteria for inclusion were:

- (1) All Children whose parents had consented to participate in the study.
- (2) Patients aged between two months and five years.
- (3) All patients admitted via AO1 to admission wards and onto the general paediatric wards.
- (4) All children, whether on first admission or re-admission to the hospital.

The criteria for exclusion were:

- (1) Children below two months and those above five years of age.
- (2) Out -patients.
- (3) Admitted patients whose parents did not consent to participate onto the study.
- (4) Patients not admitted via admission ward.

3.4. Management Of Children.

Parents of children invited to participate in the study were asked to sign an informed consent after the purpose the study has been explained to them. They were interviewed, and their children examined. The information obtained was recorded by using a standard questionnaire. By using the Zambian clinical diagnostic criteria for HIV infection, patients were divided into two groups; those who were suspected to have the disease and those not (unsuspected) suspected. To both groups voluntary HIV counselling and antibody testing was provided. Both pre- and post-counselling was done for both HIV positive and negative children. Blood for HIV testing was only taken from children whose parents had consented to an HIV test, whether the HIV infection was suspected or not. HIV antibody test was initially screened with the Capillus rapid test and confirmed by using ELISA test. The clinical diagnosis was made and its outcome (survival to discharge or death) known whilst in the ward.

The following working definitions for common diagnosis were used.

- (1). Pneumonia: - the presence of respiratory symptoms and signs for less than two weeks'

Duration. Presence of shadowing on chest x-ray.

- (2). Tuberculosis (T.B): - the paediatric criteria used at UTH. The presence of three or more of

The following satisfies a clinical diagnosis of Tuberculosis:

- a. Symptoms and signs suggestive of T.B - chronic cough, un-resolving pneumonia, wasting, persistent fever, night, sweats, etc.
- b. Sputum smear or gastric washings positive for acid-fast bacilli.
- c. Lymph node or other tissue biopsy revealing acid-fast bacilli or suggestive of TB.
- d. Radiological features suggestive of TB.
- e. Response to anti-TB treatment.
- f. History of close contact with a case of TB.

- (3). Protein Energy malnutrition (PEM): - This was defined by the Welcome criteria as follows:

Underweight, Marasmus, Kwashiorkor and Marasmic- Kwashiorkor. Underweight child was defined as one whose weight is between 60% and 80% of the normal body weight, without oedema. Marasmus was diagnosed if a malnourished child had weight less than 60% of the normal body weight for age with no oedema.

Kwashiorkor was in a child weighing between 60% and 80% of normal weight for age, with Oedema. A malnourished child was said to have Marasmic- Kwashiokor when he/she presented with a combination of signs and symptoms of Marasmus and Kwashiorkor.

- (4). Diarrhoea – This was defined as the passage of three or more loose stool in 24 hours, according to the standard WHO definition of Diarrhoeal Diseases. Acute Diarrhoea disease was defined as diarrhoea of less than two weeks duration. Persistent diarrhoea was defined as diarrhoea that lasted for two weeks or more and is of infectious aetiology.

- (5). Malaria - strong suspicion based on clinical symptoms plus either parasites on blood

film or prompt response to anti-malaria therapy

(6). Others - clinical diagnosis of other disease besides the ones mentioned above.

3.5. Sample Size.

To determine a significant difference between the two groups, in this case comparison rates, the mortality rate between HIV positive children and HIV negative children admitted to one of the wards at the University Teaching Hospital. The following formula allowed us to calculate sample size required with, a likelihood of 90% confidence, to determine a significant result between the two groups:

$$r = \frac{(u + v)^2 * (r_1 + r_2)}{(r_1 - r_2)^2}$$

Where, n = sample size of interest

r_1 = mortality rate for HIV + group

r_2 = mortality rate for other group of children

u = one-sided limit of the normal distribution, corresponding to 1000% - the power. The power is defined as the probability to detect significant difference.

v = tow-sided limit of the normal distribution, corresponding to the two-sided

Significance level.

For this analysis the mortality rate was estimated from the data collected from the study conducted at the University Teaching Hospital by C. Chintu et al concerning the impact of HIV on common Paediatric lives in Zambia. It was found that the mortality rate for the HIV positive group was 190 per 1000 children admitted, and was 100 per 1000 children admitted for the other group of children admitted. Therefore, the required sample size to determine a significant difference between the two groups at a significance level of 90% is given below:

$$\begin{aligned} n &= \frac{(1.28 + 1.96)^2 * (190/1000 + 100/1000)}{(190/1000 - 100/1000)^2} \\ &= 376 \end{aligned}$$

From the above calculations therefore, the total number of children required to achieve the level of significance desired was 376. This study recruited 502 children, 413 of whom consented to HIV testing and 404 yielded results.

3.6. Ethical Issues

Parents of the children admitted were given verbal and written information and those consenting were asked to sign. Voluntary counselling was undertaken with all children's parents and HIV antibody testing performed only on those whose parents /guardians had consented. This study was approved by the Research Ethics committee of the University of Zambia.

3.7. Data Analysis.

Information collected in this study was entered and analysed by using EPI INFO. 6.0 software. Odds ratios, chi squares and p-values were used.

3.8 LIMITATIONS OF THE STUDY

1. The study would have been better if mothers were also tested for the presence HIV antibodies in their blood. This was not done due to financial constraints since the virology laboratory could not allow us to use their reagents.
2. Determining the socio-economic status of the family was difficult because very few were willing to give information concerning the family income. Moreover, a good number of children were either brought to the hospital by grandmothers or some other relatives. It would have been better if fathers were interviewed as well.
3. A large sample size would have been more representative. This is because most of the children in this study were aged below 18 months. This problem arose because the sample size was not calculated using the children aged above 18 months.
4. Diagnostic laboratory tests (PCR) were not done in the confirmation of HIV disease in children aged less than 18 months old.

CHAPTER 4.

4.0. RESULTS

During the study period total of 3410 children were admitted. Out of these, 502 children were aged between two months and five. The results revealed that 413 (83%) parents consented their children's HIV testing. At the time of analysis, only 404 results were available and the remaining nine were indeterminate .The results for both HIV positive and negative children are shown in the below:

Table 1. Serostatus Of The Study Population

SEROSTATUS	N° OF CHILDREN	PERCENTAGE (%)
Positive	158	39
Negative	246	61
TOTAL	404	100

Table1.shows that in the study population, 158 (39%) children tested HIV positive while 246 (61%) tested negative. The percentage of the serostatus in this table does not represent the true prevalence of HIV since it includes even children aged below 18 months.

Table 2. Age Distribution And HIV Serostatus

AGE (MONTHS)	NO.OF CHILDREN (%)	N0. OF HIV POSITIVE (%)
2 - 5	50 (12.4)	25 (50)
6 - 11	106 (26.2)	31 (29)
12- 17	80 (19.8)	32 (40)
18- 23	57 (14.1)	22 (39)
24- 29	49 (12.1)	20 (41)
30- 35	22 (5.5)	10 (45)
36- 41	11 (2.7)	4 (36)
42- 47	10 (2.5)	4 (40)
48- 53	7 (1.7)	4 (57)
54- 59	12 (3.0)	6 (50)
TOTAL	404 (100%)	158

Table 2 shows that the majority of the children were aged between 6 and 11 months (26.2%), and 12 and 17 months, (19.8%), respectively. The HIV seropositivity was highest in age group between 48 to 53 months, (57% of children), followed by ages between 54 to 59 and 0 to 5 months, with 50% of children in each group being positive. From ages below 18 months some of the uninfected children tested may have positive as a result of persisting maternal antibodies.

Table 3. Sex Distribution And HIV Serostatus

SEX	No. OF CHILDREN (%)	No. SEROPOSITIVE (%)
Female	230 (57)	80 (35)
Male	174 (43)	78 (45)
Total	404 (100)	158

The Table above shows that from the study population, 57% were female while the remaining 43% being males .The female to male ratio was 1.3:1 Out of 230 female children, 80 (35%) of

them had tested positive to HIV antibodies. From 174 male children 78 (45%) of them had tested HIV seropositive. These results therefore show that HIV seropositivity was significantly higher in males than in female children, (P –value of 0.014).

Table 4. Distribution Of HIV Serostatus Between Children Aged Below 18 And Those Aged Above 18 Months

AGE (MONTHS)	HIV SEROPOSITIVE (%)	TOTAL (%)
Below 18	97 (38)	252 (62)
Above 18	61 (40)	152 (38)
Total	158	404 (100)

From the total of 404 children recruited into the study, 252 (62%) were aged below 18months while 152 (38%) being above 18 months of age. The HIV results from table 4 show that 97 (38%) children aged below 18months had tested HIV seropositive, and so were 61(40%) children aged above 18 months. The difference in serostatus between age groups was not statistically significant (P- value ,0.744) .

4.1. Hospital Admissions.

Table 5.: Relationship Between HIV Serostatus And The Number Of Previous Admission

(a) Children below 18 months

HIV STATUS	TOTAL N ^o .	N ^o OF PREVIOUS ADMISSIONS			PERCENTAGE (%)
		1	2	3 or MORE	
Positive	91	22	6	2	26
Negative	161	37*	4	6	29
Total	252	59	12	6	

(b) Age above 18 months

HIV STATUS	TOTAL N ^o	N ^o OF PREVIOUS ADMISSIONS			PERCENTAGE (%)
		1	2	3 or MORE	
Positive	61	30	6	3	64
Negative	91	23	0	0	25
Total	152	53	6	3	

Table (5a) shows that there was no significant difference in the number of previous admissions between the HIV positive and negative children aged below 18 months. Table (5b), representing the children aged above 18 months showed a significant difference in the number of previous admissions between HIV negative and positive children, (P-value, 0.32)

Table 6. The Relationship Between HIV Serostatus And Major Diseases Among Children In The Study Population.

(a) Below 18 months Old

DISEASE	TOTAL	HIV POSITIVE (%)		ODDS RATIO	95% CI
Pneumonia	66	28	(42)	1.249	0.776-1.787
PEM	22	11	(50)	1.674	0.721-3.543
TB	14	7	(50)	1.422	0.502- 4.030
Diarrhoea	69	25	(36)	0.876	0.596-1.382
Malaria	30	6	(20)	0.340	0.169-0.942
Other	51	20	~ (39)	1.039	0.624-1.702
TOTAL	252	97			

(b) Above 18 months

DISEASE	TOTAL	HIV POSITIVE (%)	ODD Ratio	95% CI
Pneumonia	33	12 (36)	0.851	0.470 - 1.653
PEM	48	22 (46)	1.486	0.821 - 2.075
TB	12	9 (75)	5.280	1.306 - 16.39
Diarrhoea	18	9 (50)	1.640	0.650 - 3.659
Malaria	26	4 (15)	0.228	0.101 - 0.772
Other	13	3 (23)	0.434	0.132 - 1.612
TOTAL	150	59		

Table (6a) shows that for children who were aged below 18 months, the HIV sero-positivity was higher in those who were admitted with PEM (50%), TB (50%) and Pneumonia (42%). For the children aged above 18 months, as in Table (6b), HIV sero positivity was significantly higher in those with TB (75%), diarrhoea (50%), PEM (46%), and Pneumonia (36%), respectively. Malaria had the lowest sero prevalence in both age groups. In the same age group two HIV sero positive patients had presented with a combination of TB and Malaria. In group 6(a), all the children that presented with diarrhoea, was of less than two weeks duration (acute diarrhoea) . In the later group, (6b), three out of 18 had presented with diarrhoea lasting for more than two weeks (persistent diarrhoea) and were all HIV positive.

4.2. Hospital Outcome.

Table 7. Shows The Relationship between Serostatus And Hospital Outcome

(a) Below 18 months

SEROSTATUS	DISCHARGES (%)	DEATHS (%)	TOTAL
Positive	76 (78)	21 (22)	97
Negative	133 (86)	22 (14)	155
Total	209	43	252

Mortality Rate: HIV positive = 22%, HIV negative = 14.2% , P – value=0.286

(b) Above 18 months

HIV SEROSTATUS	DISCHARGES (%)	DEATHS (%)	TOTAL
Positive	48 (79)	13 (21)	61
Negative	82 (90)	9 (10)	91
Total	130	22	252

Mortality Rate HIV positive = 21%, HIV negative = 10%, P-value = 0.05

(c) All children in the study

SEROSTATUS	DISCHARGES (%)	DEATHS (%)	TOTAL
Positive	124 (78)	34 (22)	158
Negative	215 (87)	31 (13)	246
Total	329	65	404

Relative Risk - 1.715, p – 0.017, 95% CI - 1.10 - 2.6

In both age groups as shown in tables 7(a) and 7(b) mortality rates were higher in HIV positive children than those who were HIV negative, mortality rates being 22% and 21% in age groups (a) and (b) respectively. P –values were 0.286 for age group below 18months and 0.050 for that above 18 months. When all under five children were considered, as in Table 7(c), the mortality rate was still higher in the HIV positive group (22%), and the Relative Risk (RR) was such that patients who tested HIV positive were 1.7 times more likely to die than to be discharged than those who were HIV negative.

Table 8. Association Between Causes Of Death And HIV Seroprevalence

(a) Below 18 months

CAUSES OF DEATH	SERO POSITIVE			SERO NEGATIVE			MORTALITY
	Total	N° of death	(%)	Total	No of death	(%)	TOTAL (%)
Pneumonia	28	8	(29)	38	9	(34)	26 %
PEM	11	4	(36)	11	0	(0)	18%
TB	7	1	(14)	7	4	(57)	36%
Diarrhoea	25	6	(24)	44	9	(20)	22%
Malaria	6	1	(17)	24	0	(0)	3.3%
Other Diseases	20	1	(5)	31	0	(0)	2.0%
Total	97	21		155	22		

(b)Above 18 months.

CAUSES OF DEATH	SERO POSITIVE			SERO NEGATIVE			MORTALITY
	Total	N° of death	(%)	Total	No of death	(%)	TOTAL (%)
Pneumonia	12	3	(25)	21	2	(9.5)	15%
PEM	22	5	(23)	26	2	(7.7)	15%
TB	9	0	-	3	0	-	-
Diarrhoea	9	2	(22)	9	2	(22)	22%
Malaria	4	0	-	22	0	-	-
Other Diseases	3	3	(100)	10	3	(30)	46%
TOTAL	56	13		91	9		

Table 8 (a) shows that the commonest cause of death in HIV sero positive children aged below 18 months were malnutrition (36%), Pneumonia (29%), diarrhoea (24 %), and malaria (17%). For the older HIV sero-positive children, as shown in Table 8 (b), the commonest cause of death were other diseases not mentioned in the study (meningitis, septicaemia and encephalitis),

followed by pneumonia (25%), malnutrition (23%) and diarrhoea (22%). Of all the children who died of Diarrhoeal Disease, only three had persistent diarrhoea. All of these were older than 18 months and had also tested HIV positive.

Table 9. Association Between The HIV Seropositivity And Deaths Of Siblings In The Family

SEROSTATUS	TOTAL	No OF CHILDREN WITH AT LEAST 1 SIBLING	No OF DEAD SIBLINGS IN FAMILY			CHILDREN WITH DEAD SIBLINGS (%)
			1	2	3 or MORE	
Positive	158	155	38	21	8	43%
Negative	246	233	46	18	18	33%
Total	404	388				

P-value = 0.26

Table 9 shows that out of 404 children in the study group, 388 had siblings in the family. From this number, at least 67 (43%) of HIV positive children had given a history of a dead sibling in the family 39 (58%) HIV positive children had given a history of losing two siblings in the family. These results were statistically significant compared with those of HIV negative children.

CHAPTER 5

5.0. DISCUSSION

5.1. Study Population

This study was conducted in 1999 during the period between August and October. The study revealed that out of the 502 under five children whose parents/guardians were counselled for voluntary HIV testing, 83 % of them had consented for the blood test. This acceptance rate was very significant probably as a result of increased Health Education concerning HIV disease and its transmission. The study also showed that 58% of the children in the study group were aged below 18 months. The sex distribution was that females were more than males in the ratio of 1.3:1.

The overall HIV sero-prevalence in children aged less than five. This percentage was higher compared to other studies done in 1991 at UTH (M.Med. Dissertations) by C. Luo and M. Sitali in 1996 in which the seroprevalence rates were 23.9% and 30.4%, respectively (32,33). There was no significant difference in the HIV seroprevalence between age groups below 18 months and above 18 months. The true HIV seroprevalence rate of children admitted to the U.T.H in this study was represented by the serostatus rate of the children aged above 18 months, which was 40%. This high HIV seroprevalence rates among hospitalised children has been increasing over the years. Indirectly this would mean that the prevalence of maternal HIV infection has also increased or that children are living longer. The HIV serostatus of children aged below 18 months was 38%. The true seroprevalence in this age group is probably lower than 38%, because some of them may still be carrying maternal HIV antibodies, although some children may actually be infected with HIV. The serostatus of Children aged less than 18 months depicts the number of children who have been perinatally exposed to the maternal HIV infection, and are therefore coming from HIV/AIDS affected families. Paediatric HIV infection

is largely influenced by the infection in the mother.

This means that a high HIV seroprevalence in antenatal mothers will lead to more children being born with HIV infection. Most of the children who acquire HIV infection early in life tend to die early due to the fast progression of the disease. At UTH the seroprevalence rate among antenatal mothers was 30- 40% according to the study done by Hira et al 1990, and another similar study done in Zaire (9,16). This study also revealed that HIV positive children were more likely to have had previous admission than the negative ones.

5.2. Disease Presentation

The impact of common diseases on HIV sero positive children was analysed as shown in Table 6. Malnutrition (50%), Tuberculosis (50%) and Pneumonia (42%) were among the common causes of admissions in age group below 18 months, while Tuberculosis (75%), Diarrhoea (50%), Malnutrition (46%), and Pneumonia (36%) were the commonest in age group 18 months and above. The disease pattern of children older than 18months reflected the true picture of common infections affecting children with underlying HIV infection. The overall common causes of hospital admission among under-five HIV positive children were TB, Pneumonia and PEM. Malaria was not among the commonest cause of admission in HIV positive children. The number of TB patients could have been more than what is indicated in this study. This is so because Tuberculosis is very difficult to diagnose in children and also since this is a chronic disease most patients are treated on outpatient basis at local centres. The number of children who were admitted with diarrhoea disease in both age groups was high irrespective of the HIV sero-status. This could be because the study was conducted during the diarrhoeal season. This disease pattern is similar to the 1991 study conducted by C. Chintu et al (34). In this study the common causes of infection in HIV positive under five children were TB, Malnutrition, Pneumonia and Diarrhoea, respectively Other studies done had also shown similar results

(35,36). The other diseases referred to in the study meant those not mentioned above. These included diseases such as septicaemia, meningitis, encephalitis, poisoning, congenital diseases and also patients who still under investigation.

5.3. Hospital Outcome

The hospital outcome was analysed in terms of discharges, deaths, and causes of death between two age groups. Out of the 404 under-five children recruited in this study, the mortality rates were higher in HIV sero positive children in both age groups. The mortality rates were 22% for the children aged below 18 months and 21% for the older age group. The overall mortality rate in the study population was 22% with a relative risk odds ratio of 1.715 as shown in Table 7(c). These results are comparable to other studies done at UTH and elsewhere.

The most common causes of death in HIV positive children aged below 18 months old were malnutrition (36%), pneumonia (29%), diarrhoea (24%) and malaria, respectively. Pneumonia was also the commonest cause of death in HIV negative children in the same age group. For the HIV positive children aged 18 months and above, the common causes of death were other serious infections not mentioned in the study, then followed by Pneumonia (25%), malnutrition (23%) and Diarrhoea (22%). The overall common causes of death in HIV positive children were malnutrition, Pneumonia, and diarrhoea. Although TB was among the common causes of admission in HIV positive children it was not among the common causes of death. This observation was also shown in the study conducted by C. Osborn et al in 1995 (37,38,). The reason given at the time was that although TB does not appear to be a major cause of paediatric hospital morbidity and mortality in Zambia, its contribution to childhood morbidity and mortality may be hidden under the leading causes such as pneumonia, malnutrition and diarrhoea. The number of patients who presented with malnutrition was less compared to the actual Hospital admissions because most of the children diagnosed with malnutrition are

admitted straight to the ward, only a few pass through the admission ward where the recruitment for the study patients was done. It is also important to note that the common cause of death in the HIV positive children (both age groups) were the same as those for the negative group, although the mortality was higher in the former group. These findings were similar to the necropsy descriptive study done at the U.T.H by C.Chintu et al between 1997 and 2000 in which they described the common cause of death in children as severe pneumonia (39). Although studies have shown that PCP is one of the common causes of morbidity and mortality in HIV positive children especially those below the age of one year, it was not looked for specifically in this study due to limited investigative capabilities. In this study PCP was included under the pneumonias, a disease that had contributed greatly to the mortality in this study, especially in the age group below 18 months (40).

The last table in the study (Table 9) revealed an equally important finding to this study. The results showed that 43% of HIV positive children had lost at least a sibling or more in the family. Further analysis revealed that 58% of children had lost at least two siblings or more in the family. This was an interesting finding which needed further exploration as part of the history, which in turn could be used as part of information in the definition of the clinical criteria for making the diagnosis of paediatric HIV/AIDS.

CHAPTER 6.

6.1 CONCLUSION

This study has shown that many people in the community are aware of HIV infection, and are willing to have their children tested for the presence of the HIV antibodies in the blood. This was demonstrated by the fact that 83% of parents consented to have their children's blood be tested for HIV. The problem of HIV disease is getting worse every year despite health education campaigns and other preventive put in place, as shown by the 39% overall sero-prevalence rates. This study has revealed that about 40% of hospitalised children are probably infected with HIV infection. This was supported by the sero-prevalence of children aged above 18 months (confirmed group). The most common causes of hospital admission in HIV positive under five children were Malnutrition, Tuberculosis, pneumonia and diarrhoea, respectively. Most of these children had previously been admitted to the hospital. The mortality rate was higher in the HIV infected group and in the HIV perinatally exposed (age below 18 months). The common causes of death in infected children aged less than five years admitted at the U.T.H children's wing were Malnutrition, Pneumonia and diarrhoea. Most of the HIV positive children in the confirmed group had at least a history of a death of a sibling in their family, probably due to HIV infection. Finally, in this study it was observed that in the absence of information about maternal serostatus the impact of HIV on childhood morbidity and mortality in hospitalised children below 18 months of age does not appear to differ much from that of HIV negative children of the same age group.

6.2 RECOMMENDATION

1. Despite increased health education campaigns concerning the dangers of unprotected sex, mother to child HIV transmission is still on the increase. This has been shown by the 40% HIV seroprevalence in children aged above 18 months. This study has also shown that 38% of children aged less than 18 months of age have been perinatally exposed. This finding signifies that there are many more mothers in the community who are infected with the virus. This means that there is need to implement more aggressive strategies so as to reduce the primary HIV infection in the parents.
2. In order to reduce transmission of infection to children there is need to inform the community on the importance of knowing their HIV status and on the availability of counselling and HIV laboratory testing facilities. For antenatal mothers who test positive they should be informed about the available interventions so as to reduce the Mother To Child Transmission (MTCT) of the HIV infection.
3. There is need to improve our diagnostic capabilities so that HIV infection could be diagnosed early, especially in children aged below 18 months. This can only be done by using better/modern diagnostic facilities e.g. PCR.
4. Protocols for using in the management of common diseases in HIV infected children need to be developed.

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APPENDIX

A. Consent Form

The main objective of this study is to determine the impact of HIV/AIDS on childhood morbidity and mortality among under-five children hospitalised at UTH. This study is going to involve under-five children admitted to the children's wing of the University Teaching Hospital (UTH). All the recruited children will follow up in the wards during the current admission. Voluntary counselling and HIV testing will be provided to both Parents and children who will be invited to participate in the study. Parents/guardians of the children will be interviewed before asked to sign a consent form.

I.....consent to my child's blood being taken for testing as to whether it contains HIV which causes AIDS .Before signing this form I had the opportunity to be informed about the testing and the counsellor has explained to me that further information will be given to me if I want to know the results .I understand that the results of this study will kept confidential and released only to the health staff working on this project where necessary for subsequent support .

My signature below means that I have read the consent (or consent form read to me) and I have had the opportunity to ask questions which were answered to my satisfaction .

Parent's Signature.....

B. Questionnaire

for children with a clinical diagnosis of retroviral disease

March 1999

Please give all date as dd/mm/yy

Names:	Date of birth ___/___/___	Clinic Number
---------------	----------------------------------	----------------------

A: Information from the family at discharge

1. Is the child's residence (tick one)?

a) Lusaka [] name of area.....

b) outside Lusaka []

2. Who is the main carer for the child? mother [] father [] other []

Please give details.....

3. Previous hospital admission

APPROXIMATE DATE	HOSPITAL	REASON FOR ADMISSION

B Details of present admission

Date of admission: ___/___/___

5. Was the child discharge from hospital?

Yes []

No []

If yes, please give the date of discharge: ___/___/___

If no, please give the date of death: ___/___/___ or date child and carer absconded: ___/___/___

6. Was the inpatient diagnosis?

Diarrhoea Yes []

No []

Respiratory infection

Yes []

No []

Tuberculosis Yes []

No []

Other infection

Yes []

No []

Please give details _____

7. Were the following criteria for diagnosis present?

candidiasis Yes []

No []

Respiratory infection

Yes []

No []

failure Yes []

No []

other infection

Yes []

No []

lymphadenopathy Yes []

No []

other

Yes []

No []

give details _____

8. Has the child had an antibody test? Yes []

No []

If yes, what was the result and where was the test done? _____

9. Was the child on oral co-trimoxazole at discharge? Yes []

No []

If 'yes' give duration _____

10. Comments

ANNEX

C Family History

1. Health status of mother

- a) Healthy Yes [] No [] b) ill Yes [] No []
c) died Yes [] No []

If answer yes to (b) and (c) specify the illness. _____

2. Health status of father

- a) Healthy Yes [] No [] b) ill Yes [] No []
c) died Yes [] No []

If answer yes to (b) and (c) specify the illness. _____

3. Number of children in the family.

- a) Alive [] b) Dead []

D. Social Economic status of the family.

1. Mother's educational status .

- a) Primary Yes [] No [] b) Secondary Yes [] No []
c) Tertiary Yes [] No [] d) None of the above Yes [] No []

2. Is mother working ? Yes [] No []

If answer yes what type of employment.

- a) Formal Sector. Yes [] No [] b) Informal Sector Yes [] No []
(self employed)

3. Mother's marital status

- a) Single Yes [] No [] b) Married Yes [] No []
c) Divorced Yes [] No []

4. Father's educational status.

- a) Primary Yes [] No [] b) Secondary Yes [] No []
c) Tertiary Yes [] No []

E. Diagnostic criteria.

1. Was the following Zambian clinical diagnostic criteria used to make diagnosis of paediatric AIDS?

Major Signs:

- a) Recurrent oral pharyngeal candidiasis Yes [] No []
b) Recurrent fever for at least one month Yes [] No []
c) Recurrent respiratory infection Yes [] No []

Minor Signs:

- a) Chronic diarrhoea of at least one month Yes [] No []
b) Weight loss or abnormally slow growth Yes [] No []
c) Generalised lymphadenopathy Yes [] No []
d) Persistent cough of at least one month duration Yes [] No []
e) Extra pulmonary T.B Yes [] No []
f) Pneumocystis carinii pneumonia Yes [] No []
g) Confirmed material HIV 1 infection Yes [] No []

Patient will be suspected to have Paediatric AIDS if he/she presents with at least two major and minor signs .

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2. Did the child fit in the criteria? Yes[] No[]
if answer is yes, was blood taken for laboratory HIV testing? Yes[] No[]
If the answer is yes, were the results positive? Yes[] No[]

3. Does the child fit in any of of the following groups?

- a) Un Suspected Yes[] No[] b) Suspected Unconfirmed Yes[] No[]
c) Suspected Confirmed . Yes[] No[]

SIGN _____ POSITION _____ DATE ____/____/____
NAME _____ CENTRE _____