MISSED OPPORTUNITIES FOR EARLY DIAGNOSIS OF HIV IN HIV EXPOSED INFANTS AND CHILDREN 0-18 MONTHS AT KIAMBU LEVEL V HOSPITAL

BY

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DEDICATION

I wish to dedicate this research to God for His constant presence throughout my research.

To my loving and supportive husband, Victor Mwangi Maina, who encouraged me and stood by me during this journey. To our loving daughter, Zoey Lexi for being patient with me during my thesis preparation.

To my parents and siblings for the constant encouragement and prayers.

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To my family, words cannot express my gratitude to you for your support and sacrifice to complete this program. I am forever indebted to you. God bless you.

DECLARATION

This is my original work and has not been presented for the award of degree in any other university.

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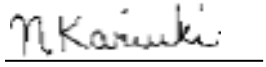
Signed:  Date: 15th November 2021

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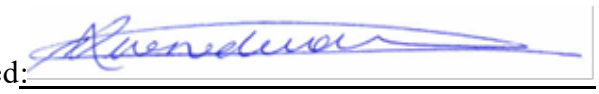
Signed:  Date: 15th November 2021

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ABBREVIATIONS

ART	Antiretroviral Therapy
AZT	Zidovudine
DBS	Dried Blood Spot
DNA	Deoxyribonucleic acid
HIV	Human Immunodeficiency Virus
IPD	Inpatient department
MH	Maternal and Child Health
NVP	Nevirapine
OPD	Outpatient department
OPH03	Optimizing Paediatric HAART 03
PCR	Polymerase Chain Reaction
PMTCT	Prevention of mother to child transmission
UNAIDS	United Nations Programme on HIV and AIDS
WHO	World Health Organization

OPERATIONAL DEFINITIONS

Child- young person of between 12 to 18 months of age.

Early Infant Diagnosis of HIV- 1st HIV DNA PCR test done within 6 weeks of age or first contact thereafter; if negative 2nd HIV DNA PCR done at 6months of age; if negative 3rd HIV DNA PCR done at 12months of age. An antibody test should be performed for all HIV exposed children at 18 months of age.

HIV exposure- infants and children born to mothers living with HIV until HIV infection in the infant or child is reliably excluded and the infant or child is no longer exposed through breastfeeding.

Infant- young child from birth to 12 months of age.

In utero: in the uterus: before birth. The term will be used interchangeably with term pregnancy.

Perinatal: period starting from 22 completed weeks to 7 days after birth.

Peripartum: period shortly before, during and immediately after giving birth.

Vertical transmission of HIV: transmission of HIV from mother to child either through pregnancy, during birth or during breastfeeding.

Serological test: identifies HIV antigen and/or antibody generated as part of the immune response to HIV infection.

Virological test: test used to detect the presence of viral nucleic acid (i.e viral RNA or viral DNA) or viral products.

ABSTRACT

Introduction: Without treatment only half of perinatally infected children celebrate their second birthday. Early detection of HIV infection, and initiation of anti-retroviral therapy (ART) treatment by 7 weeks of life has been has been shown to reduce death and disease progression by 76% and 75% respectively.

Objectives: The primary objective was to determine the prevalence of missed opportunities for early diagnosis of HIV in exposed infants and children 0-18 months of age at Kiambu level V Hospital. The secondary objectives were: to identify factors associated with missed opportunities for early HIV diagnosis and repeat testing as per guidelines and proportion of HIV infected children 0-18 months who are linked to comprehensive care.

Methodology: It was a retrospective cross-sectional study based on a review of case records of HIV1 infected women and their babies enrolled into the PMCT services between January 2017 and December 2019 and received postnatal care in the facility. The case records of the target population were reviewed to eligibility cases. HIV exposed infants/children were excluded from the study if they had transferred in to the facility at age more than 6 weeks of, transferred out of the clinic within the study period or were on transit. Clinical records were reviewed to determine whether the exposed infant accessed HIV testing as per the current guidelines. Assuming a 31 prevalence of missed opportunity for EID and using Fischers formula the samples size was computed to be of 328 mother- infant pairs. Permission to conduct the study was obtained from the KNH-ERC and the Kiambu County Hospital administration.

Results: Mother-infants pairs included in the study were 362. The median age of the babies at enrolment was 6 weeks (IQR 6.6-6.0 weeks). Overall, 51.9% of the children were male and 48.1% were female. The mean age of the mothers was 30.5 years (SD 5.7). The prevalence of missed opportunities for early diagnosis of HIV (at 6 weeks of age) was 14.9% (95% CI 81.5-88.7) and it was noted that 99.2% of the infants had contact with health care worker at 6 weeks of age during immunization. Factors that were associated with missed opportunities for early diagnosis of HIV were: entry point through the inpatient ward; mothers who ART was initiated at same time infant was enrolled and mothers who had no viral load done at time of infant's enrolment. Infants tested at 6 weeks of age who were found to be HIV infected were 2.9%. Only 77.8% of all HIV infected children 0-18 months of age were started on ART. Only 78.8%

of all the HIV exposed children had all three HIV DNA PCR tests done (at 6 weeks, 6 months and 12 months respectively) and HIV antibody test done at 18 months of age.

Conclusion: The prevalence of missed opportunities for early infant diagnosis of HIV was low at 14.9% but could have been lower as 99.2% of infants had contact with a health care worker at 6 weeks of age during immunization. Infants had increased risk of missed opportunity of early diagnosis if they identified at point mother was initiating ART, mother's lacked a viral load assessment, or identified during admission for inpatient care. At 6 weeks of age 2.9% of the infants were found to be HIV infected but only 77.8% were linked to ART treatment. Only 78.8 of the HIV exposed infants were screened for infection at the 4 recommended time points, HIV DNA PCR tests at 6 weeks, 6 months and 12 months respectively and HIV antibody test at 18 months.

Recommendations:

1. To ensure that at infant's 6 week vaccination, both the mother and infant's HIV status should be known to avoid delay in early diagnosis of HIV.
2. All patients 0 to 18 months of age admitted in the ward should have a HIV test done as soon as possible to avoid missing any opportunity for early diagnosis and early initiation of treatment.
3. Development of strategies to ensure all HIV exposed infants/children have all four tests done by 18 months of age.
4. Qualitative study with staff at the facility should be considered in future studies to determine the challenges experienced in following guidelines and specifically making sure that no HIV exposed infant/child misses an opportunity for early diagnosis of HIV.

CHAPTER 1: INTRODUCTION

HIV AIDS is a major cause of infant and childhood mortality and morbidity in Africa. HIV virus infects and destroys CD4 T helper cells (1). This depletion leads to uncontrolled viral replication with resultant viremia. Africa has a greater mortality rate among children infected with HIV compared with industrialized countries due to high burden of inter-current infection, poor nutritional intake, inaccessibility to basic healthcare, late diagnosis and inaccessibility to primary HIV care and antiretroviral therapy (ART) (1).

According to United Nations Programme on HIV and AIDS (UNAIDS) global fact sheet 2020, there were 38 million people living with HIV in 2019, 81% of them knew their HIV status, 67% were accessing ART and 59% were virally suppressed (2). Only 53% of children living with HIV were receiving lifelong ART (2). Number of people newly infected with HIV were 1.7 million, more than three times the target of 2020 which is to reduce new cases of HIV infection to less than 500,000 (2). Children (0-14 years of age) accounted for 9% of the new infections with 84% occurring in sub-Saharan Africa (2). In order to achieve an AIDS-free generation, in 2016, the UNAIDS set an ambitious target code named 90-90-90 strategy with the goal of ensuring that by 2020, 90% of all people living with HIV will be knowing their status, 90% of all people diagnosed will be on sustained antiretroviral therapy (ART) and linked to care, and 90% of all people receiving ART will have viral suppression (2).

In Kenya, in 2019, there were 1.5 million people living with HIV of whom children accounted for 7.3% (2). Children (0-14 years) accounted for 16.2% of the new HIV infections (2). Sixty three percent of children living with HIV knew their status, 63% were on ART and 51% were virally suppressed and this was still far from achieving the 90-90-90 for diagnosis, treatment and linkage to care (2). 94% of pregnant women living with HIV were accessing ART. Target that had been set in 2018 was to have gotten 95% of pregnant women on lifelong ART(2). Kenya aims to achieve the threshold of less than 5% mother-to-child transmission rate or less than 50 per 100,000 new infections, by 2021, to be certified for having eliminated mother-to-child transmission of HIV (3).

Mother-to-child transmission of HIV, can happen during pregnancy, peripartum or through breastmilk and accounts for >95% of childhood paediatric HIV infections in sub-Saharan Africa (1). Without treatment, HIV transmission rates in utero is 5-10% ; 10-20% peripartum and 5-20% during breastfeeding respectively and giving an overall transmission rate of 30-45% (4). When mother is on adequate ART and infant initiated on preventive antiretroviral

medications, HIV transmission rate can be reduced to below 5% (5). HIV infected mothers with established infection, the probability of transmitting HIV through breast milk is about 9-16% but in those who get HIV infection after delivery, the risk of breastmilk transmission is three times that of women with established infection (29-53%) (6).

Globally, mother -to-child transmission rate at 6 weeks is at 6.8% and in Kenya it is 5%; at the end of breastfeeding globally is 12.7% and in Kenya is 11% (7). Maternal health factors can influence rate of progression of perinatal HIV disease (8). Abrams EJ et al carried out a study done in USA and revealed that children born to mothers with CD4 T lymphocytes cell count less than 200cells/mm3 or HIV-1 RNA viral load > 100,000 copies/ml developed severe disease faster than those born to mothers with less severe disease (8). Mwatha A. et al carried out a nested case control study within a randomized clinical trial of breastfeeding and formula feeding among HIV-seropositive mothers in Nairobi, Kenya. They identified maternal low CD4 cell counts 384cells/mm3, high maternal plasma HIV RNA levels 88,965 copies/ml, presence of HIV-1 DNA in maternal cervical and vaginal secretions during pregnancy, vaginal or cervical ulcers during pregnancy, breastfeeding and any exposure to breastmilk and mastitis as the correlates of HIV infection among infants (9).

To minimize vertical transmission, women living with HIV should be diagnosed, treated and have suppressed viral loads from the time of conception to the time of end of breastfeeding period and for the rest of her life (7). Retaining women on ART during pregnancy and breastfeeding is important for their own health and for preventing vertical transmission (7). HIV exposure status of an infant needs to be established early so as to diagnose HIV infection early and early initiation of ART treatment (10). If not treated, 35.2% of HIV infected infants will have died by their first birthday and 52.5% of those infected will have died by their second birthday (10). A randomized trial was done in South Africa, in 2008, on early limited ART (less than 12 weeks) versus deferred therapy (more than 12weeks) in South African infants who are HIV infected. The results showed that there was benefit in early initiation of treatment, 76% reduction in early infant death and 75% reduction in disease advancement. The study also showed that death rate was much higher in first 26 after randomization in both groups and declined thereafter. (11). A randomized clinical trial was done in Kenya between year 2007 and 2009 on compromised survival benefit of early ART when diagnosis is delayed. The results showed significant mortality in infants with acute HIV-1 infection who received HIV care by age 5 months with a 12-month survival of 66.8%. The study also showed that survival benefit with ART was compromised once infant had symptomatic HIV-1 disease and was only obvious

until over 6 months after HIV-1 diagnosis thus importance on early HIV-1 diagnosis and early initiation of ART before symptomatic disease as it is crucial for infant survival (12).

The recent WHO guidelines, published in 2016, recommend that early infant diagnosis of HIV should be done at 4-6 week of age or first contact thereafter and ART started immediately for those identified as HIV infected, irrespective of immunological or clinical stage (13). In Eastern and Southern Africa, in 2019, early infant diagnosis (EID) by 8 weeks of age was 68% (2). In Kenya, early infant diagnosis by 8 weeks of age was 68.8% in 2019 compared to 67.1% in 2010 (2).

Early detection of HIV infection allows for early commencement of treatment hence improving survival (11). Virological tests are used for HIV diagnosis in children 0-18 months and it is strongly recommended that HIV virological assays used for the purpose of clinical diagnostic testing should have a sensitivity of 95% and specificity of 98% (13). Infants born to HIV-infected mothers should have initial virological testing done at birth and 4-6weeks of age or first contact thereafter as most HIV infections acquired during pregnancy and around delivery can be identified during that period (13). The 4-6weeks time period coincides with scheduled immunization visits and co-trimoxazole prophylaxis thus many infants can be tested (13). A positive virological test signifies HIV infection but a second blood sample should be collected for confirmatory HIV result but this should not delay initiation of ART as early initiation of treatment confers benefit to the infant (13).

Ministry of Health Kenya in conjunction with National AIDS and STI Control Program (NASCOP), 2018 guidelines, recommended that HIV exposure of all children <18months of age, should be established at first contact. All infants exposed to HIV should have virological testing done at 6 weeks, 6months, 12months or any other time earlier to rule out HIV infection (14). Repeat confirmatory testing should be done for any positive result (14). HIV exposed children at 18months of age should have a HIV antibody test done to rule out HIV infection (14). Information obtained from this study on missed opportunities for early diagnosis of HIV in HIV exposed infants and children, 0-18 months of age, will help the facility involved to scale up on early identification of HIV infection and early commencement of ART to lessen HIV associated illnesses and improve survival rates (11).

CHAPTER 2: LITERATURE REVIEW

2.1 IMPORTANCE OF EARLY DIAGNOSIS OF HIV IN INFANTS

Newell ML et al carried out a study on mortality of infected and uninfected infants born to HIV-infected mothers in Africa which was a pooled analysis done in 2004. Children enrolled into the study were 3,468. Eleven percent (378/3468) of the children died. Approximately one third of infected infants died by one year and half of infected children died by two years. Mortality was linked to death of mother, low CD4 cell count <200 per microliter and HIV infection in infant (lower in those infected late) (10).

Zijenah LS et al, carried out a study on timing of mother-to-child transmission of HIV-1 and infant mortality in first six months of life in Zimbabwe, in 2004. The results showed that 249 mothers (30.7%) transmitted HIV -1 infection to their infants by 6 months of age. Three-quarters of the 30.7% transmitted HIV infection during pregnancy, around delivery and early postpartum period. This indicated earlier progression to serious disease or death compared to infants acquiring disease through breastfeeding. Infant death was greater among infected infants than uninfected. Predictors for infant death were time at which child acquires the infection, weight of infant at birth and CD4 cell counts of the mother (15).

Avy Violari et al carried out a study in South Africa, on importance of early limited antiretroviral therapy initiation versus deferred treatment in HIV-infected asymptomatic infants, in 2008. Three hundred and seventy seven infants 6-12 weeks of age with CD4 lymphocyte percentage of 25% or more were enrolled in the study. One hundred and twenty five infants were assigned to deferred therapy when the cell count dropped to less than 25% and 252 infants were initiated on treatment immediately with no delays. Overall, 66% of infants in the deferred group were started on treatment after 40 weeks of follow up. The results showed that early HIV diagnosis and early initiation of ART reduced early infant mortality by 76% and HIV progression by 75% (11).

Wamalwa Dalton et al carried out a randomized clinical trial (Optimizing Paediatric HAART 03 [OPH03]) on survival benefit of early infant ART and how it is compromised when diagnosis is made late, and this was carried out between year 2007 and 2009. Ninety-nine HIV-1 infected infants were enrolled at ages 1 to 5 months and followed up for a median of 16.1 months. Overall, there were 29 (29.3%) deaths, 12 of which occurred pre-ART with a median time to death of 11 days. Overall, the 12 month survival probability was 66.8%. Eighty (80.8%) infants were initiated on ART at a median of 14 days from time of enrolment and had a survival

probability of 77.4%. Overall rate of death for the 12 was 23.6/100 person years and among those started on ART was 14.3/100 person years. There was significant mortality in infants with acute HIV-1 infection who received HIV care by age 5 months with a 12-month survival of 66.8%. The survival benefit with ART was compromised once infant had symptomatic HIV-1 disease and was only obvious until over 6 months after HIV-1 diagnosis thus importance on early HIV-1 diagnosis and early initiation of ART before symptomatic disease as it is crucial for infant survival (12).

2.2 DETERMINANTS OF EARLY INFANT DIAGNOSIS AND TREATMENT OF HIV AMONG EXPOSED INFANTS

GM Makau et al carried out a study in Kenya to evaluate determinants of early infant diagnosis and early treatment initiation among 238 HIV exposed children from informal settlements in Nairobi, in 2015. Overall, 69.2% of the mothers were less than 30 years of age, 75% had below secondary level of education, 67.6% were married and 71.4% were of poor social backgrounds. Among 77.4% of the women a HIV diagnosis was made in the preceding year, 68.5% of them during pregnancy. Knowledge on importance of EID was poor, and only 53.8% had knowledge of prevention of vertical transmission of HIV strategies. Only 38.7% received antiretroviral prophylaxis in pregnancy and 37.4% were on antiretroviral therapy at time of interview. Majority, (63.5%) had delivered in a health facility, but only 56.7% had EID at 6 weeks. While 19.7% of infants tested HIV positive, only 10.6% of infected infants were started on treatment immediately. The main determinants of EID at 6 weeks were maternal delivery at public health facility, receiving of psychosocial support, high maternal knowledge on PMTCT, mothers on antiretroviral therapy, and mother on antiretroviral prophylaxis (16).

Kebede Bekana et al, conducted a multicentre retrospective cohort study on delay in early infant diagnosis and high loss to follow up among infants born to HIV-infected women, in Ethiopia, in 2014. The study involved three government hospitals and three health centres. A total of 266 mother-infant pairs were included in the study. Only 41% (109/266) had HIV DNA PCR test done at or before 6 weeks of age. Overall, 13.4% (35/266) were found to be HIV positive. The predictors for early infant diagnosis were: mother having prenatal care, mother having received ART during pregnancy, and place of delivery (delivery in a government hospital conferred benefit to early infant diagnosis compared to delivery at home). Maternal

age, residence, occupation, parity, maternal health conditions, and marital status were not shown to be significant associated with early infant diagnosis (17).

Gaitho Douglas et al carried out a retrospective cross-sectional study on factors associated with the timely uptake of initial HIV virological test among HIV exposed infants attending clinics within a faith-based HIV program in Kenya, between January 2015 and December 2017. Initial test was considered early if sample was taken before or within 8 weeks after birth. Infants enrolled in the study were 2020. A majority, 79% (1596/2020) had their first HIV DNA PCR test done within 2 months after birth with a median age of 6.4 weeks. Overall, HIV positivity rate at initial test, among cohort, was 1.2%. Delayed HIV DNA PCR testing for early infant diagnosis of HIV was more likely to yield a positive result. The factors that were associated with late age at first HIV PCR test were: mothers who were not on ART at time of infant's HIV PCR test and infants who had not received ARV prophylaxis to prevent vertical HIV transmission (18).

Kathy Goggin et al carried out a study in Kenya on predictors of infant age enrolment in early infant diagnosis services, in 2016. Those who were registered in the study were 756 HIV infected mothers and their infants less than 18 months exposed to HIV, followed up at six Kenyan government hospitals. Predictors were assessed in three groups: "on time" (infant <= 6 weeks of age) versus "late" (>=7 weeks) and "on time" versus "very late" (>=12 weeks of age). Overall, 73.8% of mothers were able to have their infants tested "on time" versus 25% who were not. In 4 of 6 sites most infants were tested "on time" (66-92%). Two urban sites only had 47-59% of infants getting tested 'on time'. Predictors for "late" testing were lower level of education, lack of disclosure on HIV positive status to anyone, not have been on antiretroviral therapy before pregnancy, lack of information on EID from health care staff during PMTCT, having to cover a long distance to get to the hospital, insufficient funds to come to hospital, lack of family support and stigma. Age of mother was not a predictor (19).

2.3 MISSED OPPORTUNITIES FOR EARLY INFANT DIAGNOSIS OF HIV

Udochisom C. Anaba et al conducted a prospective cohort study on missed opportunities for early infant diagnosis of HIV in rural North-Central Nigeria at 20 Primary Health Care, in 2018. Four hundred and ninety seven HIV positive pregnant women-infant pairs were registered and followed up from April 2014 to November 2017. Overall, 89.9% (445/495) of

women had data available on their deliveries. Majority, 91.2%, of infants were live-born and 98% of them had available data. Early presentation for DBS sampling according to this study was sample taken between 35 to 62 days of life. Overall, 83.6% (341/408) of infants presented for DBS sample collection at least once and 72.2% had presented between 35 and 62 days (27.8% had missed opportunity for early diagnosis). Infants who never had samples collected despite having presented to the centre were 26.4%. Overall, 81.3% (210/257) infants who were tested, had samples collected at first presentation and 18.3% on subsequent presentations. Of the 257 collected samples, only 77.4% results were available from the laboratories between three months to 28 months post collection and 2 results turned out positive and one died before initiation of treatment and the other one was lost to follow up. It was concluded that although 83.6% of infants presented for testing, missed opportunities were identified which were linked to the health system failure and included infants presenting to the health centre but not being tested, late sample collection yet patient had presented severally to the facility, long turnaround time to receipt on infants' HIV test results to the facility and patients. Of the 2 infants who tested HIV positive, none of them was linked to care which may have led to 1 mortality (20).

SA Woldesenbet et al carried out a national study in South Africa and data used was obtained from two cross-sectional surveys that were carried out in South Africa in 2010. Six hundred and twenty five public facilities were randomly selected to find out procedures for early infant diagnosis of HIV. Five hundred and sixty five of the facilities were revisited to determine intention of mothers to ask for EID service at 6-week immunization visit and the potential predictors. 10820 mother/caregivers were screened for eligibility. Only 68% of immunization service points (ISPs) provided early infant diagnosis of HIV to infants whose mothers disclosed HIV exposure or had their HIV status written in the mother to child booklet. For infants of whom mother's HIV status was not documented or written in the booklet thus exposure status not known, only few ISPs offered provider-initiated HIV testing and counselling. Only 29% of HIV positive mothers reported their status and were interviewed at ISPs and what was found out was that 45% of them had no documented HIV status on their booklets and 35% had planned to ask for EID services during 6-week immunization visit. Reasons for not reporting HIV status among the mothers were poor knowledge on vertical transmission of HIV, missed doses of medications and social stigma. Every mother was then given an opportunity to have HIV testing done on their infants but 5% did not give consent. Out of the 95% of infants tested, HIV exposed infants were 32%. Overall 38% HIV exposed infants either did not have their

HIV status written down in the booklet or their mothers had not planned to self-report HIV during 6 week immunization visit (21).

N.A Phiri et al conducted a retrospective cohort study in Northern Malawi on early infant diagnosis and outcomes of HIV exposed infants at a central and district hospital, in 2017. Four hundred and nine babies exposed to HIV from central hospital and 176 from district hospital were registered in the EID programme. Overall, 76% of registered infants in the central hospital had dried blood sample (DBS) collected and all processed and 61% had results given to the health care workers and 56% of guardians received their results. Eight nine percent of infants in the district hospital had samples taken but 9% of them were not processed and 53% had results given to the health care workers and 51% of guardians received their results. Guardians were getting results averagely after 34 days from sample collection, in the central hospital and 56 days in the district hospital which signified delays. Most HIV infected infants started treatment at 20weeks of age at the central hospital and 42weeks at district hospital. Overall, 92% of HIV positive infants were started on treatment in central hospital and 46% in the district hospital. In both hospitals, only 50% of samples were collected between 6 and 8 weeks of age with 25% samples in central hospital and 40% samples in district hospital collected late. The survival rates were high for those who had samples collected between 6 and 8 weeks and those who got back their results within 1 month of sample collection (22).

Mwanamkasi Tsutsu conducted a study on prevalence and factors associated with missed opportunities for HIV testing and diagnosis of children accessing health care services at Mbagathi District Hospital, in Kenya, in 2017. One hundred and sixty nine child-care giver pairs were recruited (children 0-14 years). Overall, 43% of guardians had not identified their children's HIV status. Majority of the missed opportunities occurred in mother and child health clinic (MCH) at 31% and outpatient clinics at 54%. Factors that were associated with missed opportunities for HIV testing were point of care (MCH, ward, clinic, and outpatient department), presence of counsellor in the clinic/ward, availability of testing kits, educational level of parent/guardian and presence of both parents (23).

2.4 LOSS TO FOLLOW UP AMONG HIV EXPOSED INFANTS

Ankunda Rogers et al conducted a retrospective study on loss to follow up (LTFU) and associated maternal factors among HIV exposed infants at Mbarara Regional Referral Hospital, Uganda, in 2020. Infants were classified as lost to follow up if they had not completed their

follow-up schedule by 18 months of age. Out of the 1624 infants enrolled at the PMTCT, 1073 were the ones who were analysed. Overall, 33% (533/1624) were dropped for lack of mother's clinical identification number, 18 (1.1%) were either dead or transferred out. Out of the 1073 who were analysed, 48% (515/1073) were LTFU by 18 months of age while out of the 558 who completed their follow up schedule, 3.6% (20/558) tested positive for HIV. The loss to follow up rates were: 24.3% at 3 months, 28.7% at 6 months, 40.6% at 12 months and 48% at 18 months respectively. The factors that were associated with LTFU were: young age of mother (especially those less than 23 years), far distance to hospital and mother not being on any family planning method (24).

Alamdo AG et al conducted a retrospective cohort study on retention in care and health outcome of HIV- exposed infants in a PMTCT cohort in Addis Ababa, Ethiopia, between December 2015 and November 2018. A total of 356 mother-infant pairs were included in the study. Majority of the infants, 80.9% (288/356) had their first HIVA DNA PCR test at 6 weeks of age and 83.1% (296/356) had a negative test result. Overall, 78.65% (280/356) of the infants had completed the follow-up period (18 to 24 months). Overall, 11.52% (41/356) of the infants were lost to follow up, 8.99% (32/356) transferred out of the clinic and 0.84% (3/356) died. Overall, 86.69% (280/324) of the HIV exposed infants in the cohort were discharged as HIV negative while only 0.61% (2/324) were HIV positive, after excluding the infants who were transferred out. Factors that were associated with LTFU were: young age of the mother and those mothers who were newly HIV diagnosed at the time of entry PMTCT (25).

2.5 STUDY JUSTIFICATION AND STUDY UTILITY

HIV AIDS is a major cause of infant and childhood mortality and morbidity in Africa. Vertical transmission of HIV (either during pregnancy, labour, delivery or breastfeeding accounts for >95% of childhood paediatric HIV infections in sub-Saharan Africa. In 2019, in Kenya, 94% of pregnant women living with HIV were accessing ART. Only 63% of children living with HIV knew their status, 63% were on treatment and 51% were virally suppressed. Early infant diagnosis of HIV by 8 weeks of age was 68.8% in Kenya in 2019. This is still far from the 90-90-90 strategy that had been set by UNAIDS, in 2016, to ensure 90% of all people living with HIV will have known their status, 90% of all people diagnosed will be receiving sustained antiretroviral therapy (ART), and 90% of all people receiving ART will have viral suppression by 2020. Between year 2017 and 2019, 450 HIV exposed infants were attended to at Kiambu Level V hospital. HIV DNA PCR testing of the infants/ children is done at the PMTCT clinic within the hospital but the laboratory does not have the capacity to run the tests thus samples are usually sent to national laboratory based within Kenyatta National Hospital. Virological testing is not routinely done in the inpatient wards, outpatient department, maternity among other departments, and only those patients referred to the PMTCT clinic are tested. It is important to diagnose HIV infection in children at the earliest time possible at least by 6- 8 weeks of age to allow for early commencement of treatment which improves survival. Early initiation of antiretroviral therapy by 12 weeks reduces HIV related illnesses by 76% and death by 75%. Kenya has come up with guidelines on early infant and children (0-18months) diagnosis of HIV to ensure no infant/child is missed out on diagnosis of HIV infection and early commencement of treatment. This study will look at missed opportunities for early diagnosis of HIV in infants and children 0-18 months of age (those who are HIV exposed) which will be helpful information to the facility involved to scale up on early HIV diagnosis to allow for early commencement of antiretroviral therapy to reduce HIV related illnesses and death due to HIV in these children.

2.6. RESEARCH QUESTION

At Kiambu Level V Hospital,

1. What is the prevalence of missed opportunities for early diagnosis of HIV in HIV exposed infants and children 0-18 months of age at Kiambu Level V Hospital and associated factors?
2. What is the proportion of HIV exposed infants and children who got all three HIV DNA PCR tests at 6 weeks, 6 months, 12 months and antibody test at 18 months?
3. What is the proportion of infants who are HIV infected by 6 weeks of age?
4. What is the proportion of HIV infected infants and children 0-18 months who are linked to comprehensive care?

2.7OBJECTIVES

2.7.1 Primary Objective

To determine the prevalence of missed opportunities for early diagnosis of HIV in HIV exposed infants and children 0-18 months of age at Kiambu level V Hospital.

2.7.2 Secondary Objectives

1. To identify the factors associated with missed opportunities for early diagnosis of HIV in HIV exposed infants and children 0-18 months of age at Kiambu level V Hospital.
2. To determine the proportion of HIV exposed infants and children who accessed the 4 recommended HIV diagnostic tests; three HIV DNA PCR tests at 6 weeks, 6 months and 12 months of age and HIV antibody test at 18 months.
3. To identify proportion of infants who are HIV infected by 6 weeks of age.
4. To identify proportion of HIV infected infants and children 0-18 months who are linked to comprehensive care.

CHAPTER 3: METHODOLOGY

3.1 STUDY DESIGN

Retrospective cross-sectional study that used data (mother-infant pairs) obtained from the medical records which was collected between the period of January 2017 and December 2019 using a standard form.

3.2 STUDY SITE

This study was carried out in Kiambu Level V Hospital. It is a government referral hospital. It is located in Township Sub-location. It has a bed capacity of 316. Number of cots are 67.

3.3 STUDY PERIOD

January 2017 to December 2019.

3.4 STUDY POPULATION

All HIV exposed infants and children 0-18 months of age and their mothers who were enrolled into the PMTCT services at Kiambu Level V Hospital from January 2017 to December 2019. Between year 2017 and 2019, 450 HIV exposed infants were attended to at Kiambu Level V Hospital.

Inclusion criteria

All HIV exposed infants and children 0-18 months of age and their mothers who were enrolled into the PMTCT services at Kiambu Level V Hospital between January 2017 and December 2019.

Exclusion criteria

1. Transfer in at an infant age of more than 6weeks.
2. Transfer out between 0-18 months of age.
3. Those infants/children that were on transit.

3.5 CASE DEFINITIONS

1 Missed opportunity for early diagnosis of HIV: infant/child who came into contact with health care worker and was eligible for HIV DNA PCR testing/ HIV antibody testing but test not done.

2 HIV exposed Infant/ child: infant/child 0-18 months of age who has risk of acquiring HIV infection (when mother is HIV infected) during pregnancy, labour, deliver and through breastfeeding. A positive HIV antibody test in child less than 18 months reveals the presence of maternal antibodies that indicate exposure to the virus, not necessarily infection by the virus. Children produce their own antibodies at around 18 months of age.

3 HIV infected infant/child: infant/child 0-18 months of age who acquires HIV infection from the mother either during pregnancy, labour, delivery or through breastfeeding. Infection confirmed with a positive HIV DNA PCR test either at 6weeks, 6 months or 12 months and positive HIV antibody test at 18 months.

4 Linkage to comprehensive care: HIV positive infant/ child enrolled to comprehensive care clinic (CCC) for initiation of treatment.

3.6 SAMPLE SIZE

The objective on prevalence of missed opportunities for early diagnosis of HIV in HIV exposed infants and children 0-18 months of age at Kiambu level V Hospital from Jan 2017 to December 2019, was used to determine the sample size, which was calculated as using the Fischer's exact formula:

$$n = \frac{Z^2 P(1-P)}{d^2}$$

n = sample size

Z = Z statistic for 95% level of confidence = 1.96

P = Estimated proportion of EID missed opportunities at 6 weeks of age = 31.2% (Kenya, 2019)

d = margin of error = 5%

$$n = \frac{1.96^2 \times 0.31 \times (1-0.31)}{0.05^2}$$

The calculated sample size was 328 mother-infant pairs.

3.7 SAMPLING PROCEDURE

HIV exposed infants, 0-18 months of age enrolled in the PMTCT clinic between January 2017 and December 2019, were screened for eligibility and those who were eligible were included into the study consecutively.

3.8 STUDY PROCEDURE

A research assistant, with a minimum qualification of diploma in clinical medicine, was identified by the principal investigator and trained on research conduct, ethics and data collection. The HEI registry book was used to identify each infant's unique HEI identification (ID) number together with the mother's unique ID number. Files were then retrieved from the records department using each infant's mother's unique ID number as each infant's HEI card was attached to the mother's file. Both mother's and infant's data is usually collected using a standard form and this minimized having any missing data. Information relevant to the study was then collected and tabulated on Microsoft excel.

Study variables

Dependent variables:

i) HIV DNA PCR testing (1st, 2nd and 3rd) and HIV antibody testing, availability of the test results.
ii) Proportion of infants who test HIV positive at 6 weeks of age.
iii) Proportion of HIV infected children 0- 18 months who are linked to comprehensive care.

Independent variables:

i) Infant/ child: age, sex, entry point, feeding option, antiretroviral prophylaxis regimen, place of delivery, immunization status.
ii) Maternal: age, marital status, education level, employment status, ART regimen, viral load at child's enrolment, place of delivery.

3.9 DATA MANAGEMENT AND ANALYSIS

Data was entered and managed in Microsoft Excel 2016 data entry sheet. Data cleaning was performed during data entry and any incomplete or inaccurate information was confirmed from the source documents. The cleaned data was then exported into SPSS version 23.0 statistical software for analysis.

The study population was described using demographic and clinical characteristics of the HEI and their caregivers. Continuous data was summarized into means with standard deviations (SDs) and medians with interquartile ranges (IQRs) where appropriate. Categorical variables were presented using frequencies and percentages.

Missed opportunities for early diagnosis of HIV in HIV exposed infants were calculated using the number of eligible infants/children in contact with the health care system but did not receive HIV DNA PCR testing. This was calculated with reference to clinic attendance when the infant/child was 6 weeks, 6 months, 12 months and 18 months of age. Missed opportunities were presented as percentages with 95% confidence interval.

HIV infection at 6 weeks was determined and presented as a percentage of all children tested at that point. In addition, linkage to comprehensive care centre was established and proportion of HIV infected children linked to treatment presented.

Children who missed early infant diagnostic test at 6 weeks of age versus those who complied were stratified by their socio-demographic and selected clinical characteristics of their mothers and the differences tested using chi square test for categorical data. Odds ratios were calculated to estimate risks of missed opportunities associated with the child and maternal characteristics. Means were compared using independent t test while medians were compared using Mann Whitney U test. All statistical tests were tested at 5% level of significance (p value less than 0.05).

3.10 ETHICAL CONSIDERATIONS

The principal investigator sought ethical approval from the Kenyatta National Hospital and University of Nairobi (Department of Paediatrics) Ethics and Review Committee (KNH-UoN ERC). After receipt of ethical approval, the proposal was presented to the Medical Superintendent of Kiambu Level V Hospital who gave his approval of the study. Consent from study participants was not sought as the study was retrospective thus records were used to

extract the relevant information to the study. Confidentiality was maintained as individual names and other identifying information was not shared with persons not directly involved in the study.

Feedback on the study findings was and will be provided to the relevant authorities at Kiambu Level V Hospital and also to the faculty and students at the Department of Paediatrics and Child Health.

3.11 QUALITY ASSURANCE

One research assistant was recruited into the study with a diploma in clinical medicine and an interest in HIV and were trained on research conduct, ethics and data collection. Multiple sources of information were available (mother's records and the HEI register) which are standardized tools and therefore standard data was collected from every mother-infant/child pair. Data abstraction forms were checked for completeness before analysis. Errors in the source document could not be corrected.

CHAPTER 4: RESULTS

A total number of 450 children 0-18 months of age with their mother pairs who were enrolled at PMTCT clinic at Kiambu Level V Hospital between January 2017 and December 2019 were screened for eligibility using the HEI registry. Overall, 19.55% (88/450) infants/children were excluded from the study due to the following reasons: transfer in for than 6 weeks of age, transfer out within the study period and those infants that were on transit thus not being followed up at Kiambu Level V Hospital. Overall, 362 mother-infant pairs were included in the study. Figure 1 below is the study flow chart showing patient enrolment:

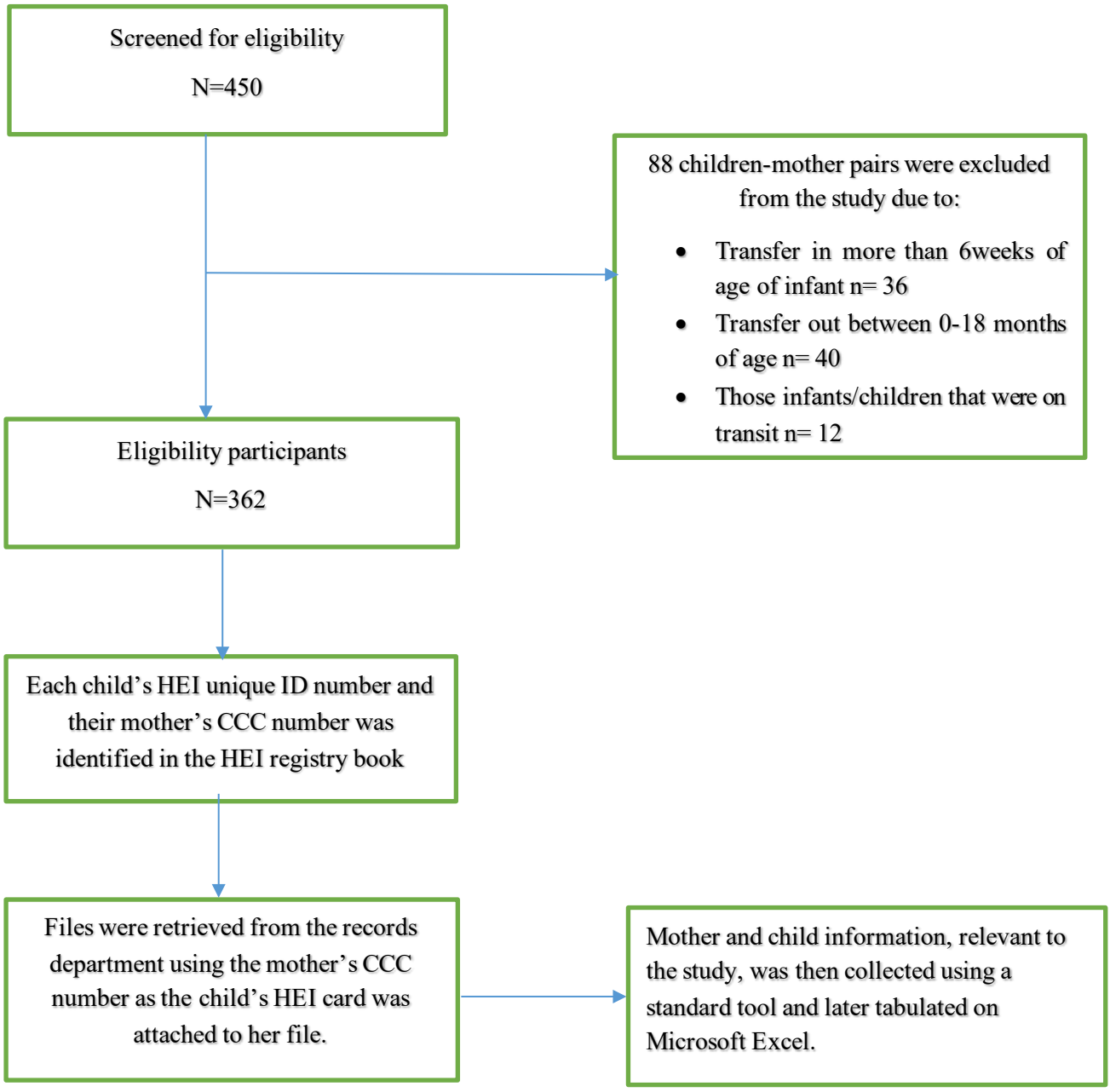

Figure 1: flow chart showing enrolment of participants in the study using file records

4.1 SOCIODEMOGRAPHIC CHARACTERISTICS OF THE INFANTS AND CHILDREN

The median age at enrolment was 6 weeks (Interquartile range of 6.0-6.0 weeks). Majority, 99.2% (359/362) of the infants had been presented to hospital at 6 weeks of age for immunization thus having contact with a health care worker. Overall, 51.9% (188/362) of the children were male while 48.1% were female. Majority of the children (82.6%) had entry point through MCH/PMTCT clinic with maternity had only referred 6 (1.7%) children referred. Overall 100% (362/362) of the mothers adhered to the Kenyan guidelines of exclusive breastfeeding for the first six months. Majority of the children, 92.6% (336/362), were delivered at a facility while 7.2% were delivered at home. Majority, 92% (333/362) of the children were on the correct ARV prophylaxis regimen according to the year they had been enrolled (NVP for 12 weeks (beginning of year 2017), NVP for 12 weeks plus AZT for 6 weeks (year 2017 to beginning of year 2018) and AZT for 6weeks plus NVP through breastfeeding (year 2018 up to date).

Table 1: Characteristics of the children

Variable	**n=362** **Frequency (%)**
Median age of the child at enrolment (IQR) in weeks	6.0 (6.0-6.0)
Sex of the infant	
Male	188 (51.9)
Female	174 (48.1)
Entry point	
1.Ward/IPD	13 (3.6)
2. OPD	10 (2.8)
3. Maternity	6 (1.7)
4. CCC	25 (6.9)

5. MCH/PMTCT	299 (82.6)
6. Transfer in	9 (2.5)
Feeding option	
Exclusive BF	362 (100)
Not BF	0 (0)
Place of delivery	
Facility	336 (92.6)
Home	26 (7.2)
ARV prophylaxis regimen	
NVP during BF + AZT for 6 weeks	151 (41.7)
NVP for 12 weeks + AZT for 6 weeks	113 (31.2)
NVP for 12 weeks	69 (19.1)
NVP for 6 weeks	8 (2.2)
NVP for 6 weeks + AZT for 6 weeks	2 (0.6)
Single dose NVP Only	2 (0.6)
NVP during BF	1 (0.3)
None	16 (4.4)
Immunization	
Up to date	312 (86.2)
Loss to follow up after 6 weeks of age	47 (13.0)
Not documented	3 (0.8)

4.2 MATERNAL SOCIO-DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

The mean age of the mothers was found to be 30.5 years (standard deviation 5.7). Overall 34.3% (124/362) of the mothers had their highest level of education as primary school while only 14.9% (54/362) had attained tertiary level of education. Half the women, 51.5% (185/362) were unemployed. There was almost equal distribution in terms of formal, self and informal employment. Overall 59.7% (216/362) of the mothers were married, 29.3% were single and 0.8% were cohabiting. The median ART duration was found to be 10.5 months. (Interquartile range 3.0-48.0). Majority of the mothers, 97% (351/362), were on first line ART regimen some of whom had been started on treatment at the same time the child was enrolled into the PMTCT clinic. Majority of the mothers, 92.6% (336/362), had delivered at a facility while 7.2% (26/362) had delivered at home. Only 42% (152/362) of the mothers had a viral load of less than 1000 copies/ml. more than half of the mothers had no viral load done at the time of infant's or child's enrolment into the PMTCT clinic.

Table 2: Maternal socio-demographic and clinical characteristics

Variable	**n=362** **Frequency (%)**
Mother's age, mean (SD) in years	30.5 (5.7)
Mother's education level	
None	66 (18.2)
Primary	124 (34.3)
Secondary	118 (32.6)
Tertiary	54 (14.9)
Mother's employment status	
Formal employment	60 (16.6)
Self-employment	57 (15.7)
Informal employment	60 (16.6)
None	185 (51.1)

Marital status	
Married	216 (59.7)
Single	106 (29.3)
Divorced	32 (8.8)
Widowed	5 (1.4)
Cohabiting	3 (0.8)
Mother's duration on ART in months	
Median (IQR)	10.5 (3.0-48.0)
Min-Max	0-144
Mother's VL at child enrolment	
<1000	152 (42.0)
>=1000	9 (2.5)
Not done	201 (55.5)
Mother's ART regimen	
First line	351 (97.0)
Second line	11 (3.0)
Place of delivery	
Facility	336 (92.6)
Home	26 (7.2)

4.3 INFANT HIV DNA PCR TESTING AND THE PREVALENCE OF MISSED OPPORTUNITIES

As per the Kenyan national guidelines, 85% (308/362) of the infants had their 1st HIV DNA PCR test done at 6 weeks and this coincided with the period when majority of the infants (99.2%) had their first contact with a health care worker and were eligible for testing and this was during immunization. Of all 362 participants, 308 were seen at the PMTCT clinic at 6-week visit and 14% (54/362) were late presenters. Nine out of the 308 infants had a positive

HIV DNA PCR result and were thus excluded from further testing. At 6 months of age, 353 (362-9 positive cases) infants were eligible for testing (1st or 2nd HIV DNA PCR test depending on time of presentation) and 89.5% (316/353) tests were done out of which 7 of the results were HIV positive and thus excluded from further testing. Overall, 10.5% (37/353) missed an opportunity for testing at 6 months of age. At 12 months of age, 346 (353-7 positive cases) infants were eligible for testing (1st, 2nd or 3rd HIV DNA PCR test depending on time of presentation) and 84.7% (293/346) tests were done out of which 6 of the results were HIV positive and thus excluded from further testing. Overall, 15.3% (53/346) missed an opportunity for testing at 12 months of age. At 18 months of age, 300 children were eligible for HIV antibody test (those excluded from this number were 35 children who had not yet attained 18 months of age and 5 children whose results were HIV positive. Of the 300 children, 74% (222/300) had the 18month antibody test as their 4th test to rule out HIV infection, 5% (15/300) had the 18 month antibody test done but not all the three HIV DNA PCR tests and thus the HIV antibody test was not their 4th test. Overall, 21% (63/300) missed the HIV antibody test as they were lost to follow up. Overall, 14.9% (54/ 362) had missed the opportunity for early diagnosis of HIV at 6 weeks of age, 10.5% (37/353) of the infants had a missed opportunity for the second HIV DNA PCR testing at 6 months of age, 15.3% (53/346) of the infants had a missed opportunity for the third HIV DNA PCR testing at 12 months of age and 21% (63/300) of the infants had a missed opportunity for HIV antibody testing at 18 months of age.

4.4 PROPORTION OF HIV EXPOSED INFANTS AND CHILDREN WHO GOT ALL THE THREE HIV DNA PCR TESTS AT 6 WEEKS, 6 MONTHS AND 12 MONTHS OF AGE AND HIV ANTIBODY TEST AT 18 MONTHS.

As shown in table 3, only 74% (222/300) of the HIV exposed children had all three HIV DNA PCR tests done (at 6 weeks, 6 months and 12 months respectively) and HIV antibody test done at 18 months of age and the results were negative. Overall, 21% (63/300) missed the 18 month HIV antibody test due to loss to follow up and 5% (15/300) had the 18 month HIV antibody test done but not all the three HIV DNA PCR tests were done.

Table 3: Infant's HIV DNA PCR testing at 6weeks, 6 months, 12 months and HIV antibody test at 18 months

Variable	Frequency (%)	95% CI
At 6 weeks (n=362)		
Done	308 (85.1)	81.5-88.7
Missed	54 (**14.9**)	11.3-18.5
At 6 months (n=353)		
Done	316 (89.5)	86.4-92.6
Missed	37 (10.5)	7.4-13.6
At 12 months (n=346)		
Done	293 (84.7)	80.9-88.2
Missed	53 (15.3)	11.8-19.1
At 18 months (n=300)		
Done (all 4 tests)	222 (74%)	69.0-79.0
Done (less than 4 tests)	15 (5%)	2.5-7.5
Missed (loss to follow up)	63 (21%)	16.4-25.6

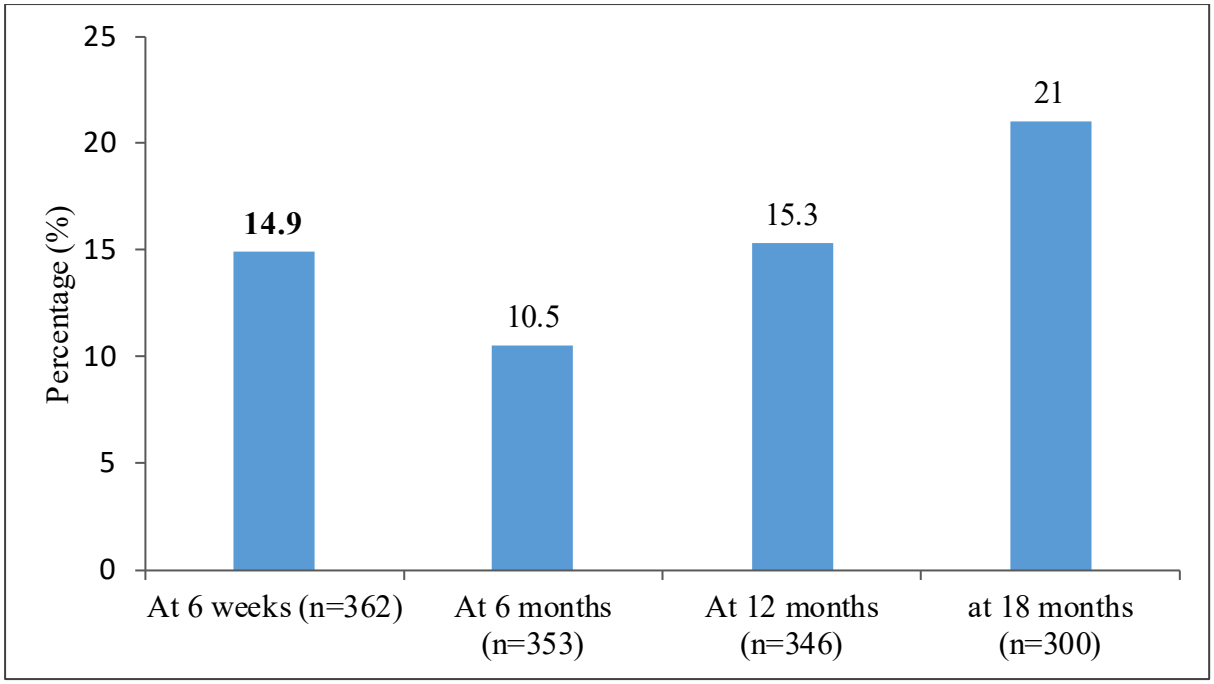

Figure 2: Missed opportunities for HIV DNA PCR and HIV antibody testing

4.5 FACTORS ASSOCIATED WITH MISSED OPPORTUNITIES OF EARLY HIV DIAGNOSIS AT 6 WEEKS OF AGE

As shown in table 3, in univariate analysis, majority of the infants who did not miss an opportunity for early diagnosis of HIV had been referred from the MCH/PMTCT clinic 87.3% (269/308) most probably owing to the fact that the period coincided with immunization. There was a 49.3 times higher odds of infant/child missing an opportunity for early diagnosis of HIV having been referred from inpatient department (IPD) versus from Mother and Child Health clinic (MCH) OR=49.3 [(95% CI 10.4-233.1) p value <0.001].

Mother's duration on ART was associated with missed opportunity for early diagnosis of HIV in the infant. Infants whose mothers were started on ART at time of their enrolment (coinciding with when the mother's HIV positive status was known) were more likely to miss an opportunity for early diagnosis compared to those mothers who were on ART for at least 12 months (p value <0.001).

In regards to mother's viral load at child's enrolment, there was a 5.2-times higher odds of an infant/child missing an opportunity of early diagnosis of HIV if the mother had no viral load done compared to those children whose mothers had viral load done and value was less than 1000 copies/ml OR=5.2 [(95% CI 2.4-11.4) p value <0.001].

Other variables that were tested but found not to be significantly associated with missed opportunity for early infant/ child diagnosis of HIV included: sex of the infant, mother's age, mother's education level, mother's employment status, mother's ART regimen, mother's place of delivery and mother's marital status.

Table 4: Missed opportunities at 6 weeks and the associated factors

Variable	Missed (n=54)	Did not miss (n=308)	OR (95% CI)	P value
Sex				
Male	24 (44.4)	164 (53.2)	0.7 (0.4-1.3)	0.232
Female	30 (55.6)	144 (46.8)	1.0	
Entry point				
MCH/PMTCT	30 (55.6)	269 (87.3)	1.0	
Ward/IPD	11 (20.4)	2 (0.6)	49.3 (10.4-233.1)	<0.001
OPD	10 (18.5)	0	-	0.999
Maternity	1 (1.9)	5 (1.6)	1.8 (0.2-15.9)	0.599
CCC	2 (3.7)	23 (7.5)	0.8 (0.2-3.5)	0.744
Transfer in	0	9 (2.9)	-	0.999
Mother's age, mean (SD)	31.4 (5.7)	30.3 (5.7)	-	0.165
Mother's education level				
None	5 (9.3)	61 (19.8)	0.8 (0.2-2.9)	0.740
Primary	22 (40.7)	102 (33.1)	2.1 (0.8-5.9)	0.154
Secondary	22 (41.7)	96 (31.2)	2.2 (0.8-6.3)	0.124
Tertiary	5 (9.3)	49 (15.9)	1.0	
Mother's employment status				
Formal employment	10 (18.5)	50 (16.2)	1.1 (0.5-2.4)	0.855

Self-employment	8 (14.8)	49 (15.9)	0.9 (0.4-2.0)	0.764
Informal employment	7 (13.0)	53 (17.2)	0.7 (0.3-1.7)	0.448
None	29 (53.7)	156 (50.6)	1.0	
Mother's duration on ART, median (IQR) in months	0 (0-4.0)	12.0 (4.0-48.0)	-	<0.001
Mother's VL (copies/ml)at child enrolment				
<1000	8 (14.8)	144 (46.8)	1.0	
>=1000	1 (1.9)	8 (2.6)	2.3 (0.3-20.3)	0.469
Not done	45 (83.3)	156 (50.6)	5.2 (2.4-11.4)	<0.001
Mother's ART regimen				
First line	53 (98.1)	298 (96.8)	1.8 (0.2-14.2)	1.000
Second line	1 (1.9)	10 (3.2)	1.0	
Place of delivery				
Facility	48 (88.9)	288 (93.5)	0.6 (0.2-1.5)	0.250
Home	6 (11.1)	20 (6.5)	1.0	
Marital status				
Married	33 (61.1)	183 (59.4)	1.0	
Single	6 (11.1)	26 (8.4)	1.3 (0.5-3.3)	0.615
Divorced	0	5 (1.6)	-	0.999
Widowed	0	3 (1.0)	-	0.999
Cohabiting	15 (27.8)	91 (29.5)	0.9 (0.5-1.8)	0.790

4.6 PROPORTION OF INFANTS/CHILDREN WHO ARE HIV INFECTED BY 6 WEEKS OF AGE

According to table 4, 2.9% (9/308) of infants who had HIV DNA PCR test done at 6 weeks of age, results turned out positive and were thus identified as having HIV infection. Overall, one third of all the HIV infected infants and children (9/27) acquired HIV infection by 6 weeks of age. Therefore 18 infant infection were late postnatal infection.

HIV infected infants at 6 months of age were 2.2% (7/316) and those infants found to be infected at 12 months of age were 2% (6/293). The proportion of children who were found to be HIV infected at 18 months of age were 2.1% (5/234). Mother-to-child transmission rate within the 3 years was 10.5% (27/256). This data is illustrated in table below.

4.7 PROPORTION OF HIV INFECTED INFANTS AND CHILDREN 0-18 MONTHS WHO ARE LINKED TO COMPREHENSIVE CARE

According to table 4, 77.8% (21/27) of infants/children identified as HIV infected were linked to comprehensive care centre (CCC) and started on ART. Overall, 22.2% (6/27) were not linked to comprehensive care out of whom 5 of them were due to loss to follow up and 1 died before linkage was done.

4.8 OVERALL STATUS OF THE IDENTIFIED HIV EXPOSED CHILDREN BY 18 MONTHS OF AGE AT KIAMBU LEVEL V HOSPITAL

Overall 71.8% (229/319) of children were HIV negative by 18 months of age. Overall, 19.7% (63/319) of children had unknown status by 18 months as they were lost to follow up. Overall, 8.5% (27/319) were HIV infected. 6.6% of those identified as HIV infected were on treatment while 1.9% were not initiated on treatment as 5 of them were lost to follow up and one of them died before linkage to comprehensive care.

Table 5: HIV infection and linkage to treatment

Variable	Frequency (%)
PCR results at 6 weeks (n=308)	
HIV-infected	**9 (2.9)**
HIV negative	299 (97.1)
PCR results at 6 months (n=316)	
HIV-infected	7 (2.2)
HIV negative	309 (97.8)
PCR results at 12 months (n=293)	
HIV-infected	6 (2.0)
HIV negative	287 (98.0)
Antibody results at 18 months (n=234)	
HIV-infected	5 (2.1)
HIV negative	229 (97.9)
Final results by 18 months of age (n=319)	
HIV-infected	27 (8.5)
HIV negative	229 (71.8)
Unknown (Loss to follow up)	63 (19.7)
MTCT rate (n=256)	
HIV-infected	27 (10.5)
HIV negative	229 (89.5)
Linkage to treatment (n=27)	
Started ART	21 (77.8)
Not linked	6 (22.2)

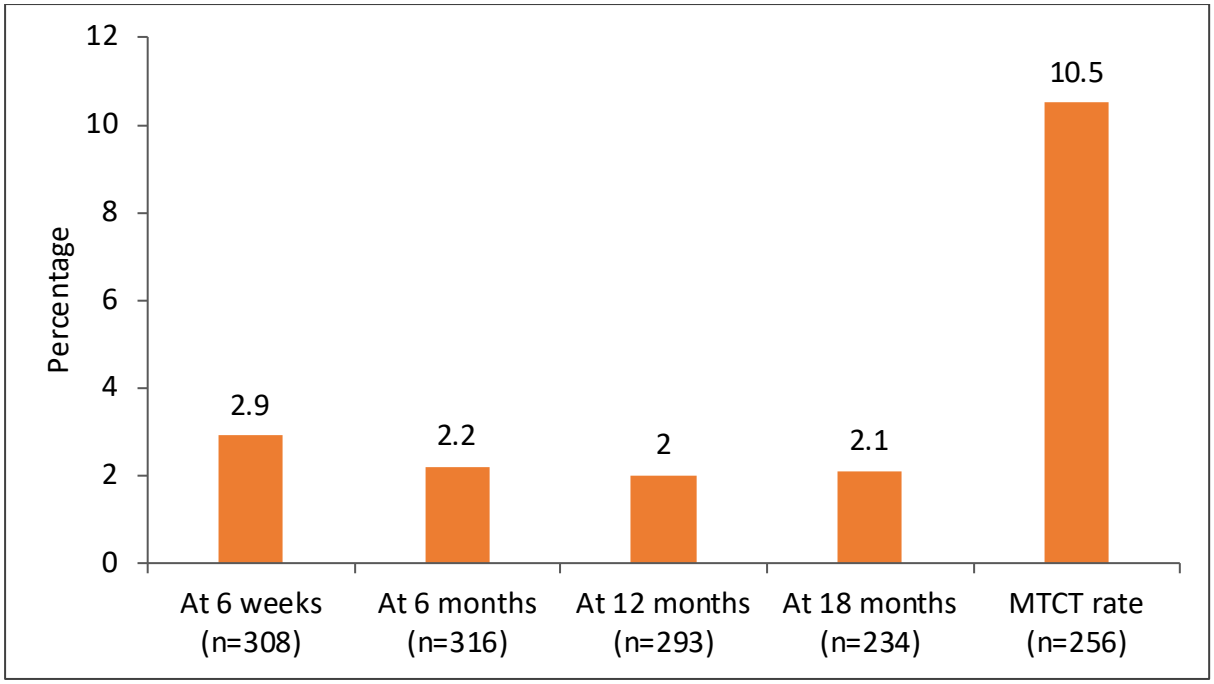

Figure 3: HIV infection rates among infants/children

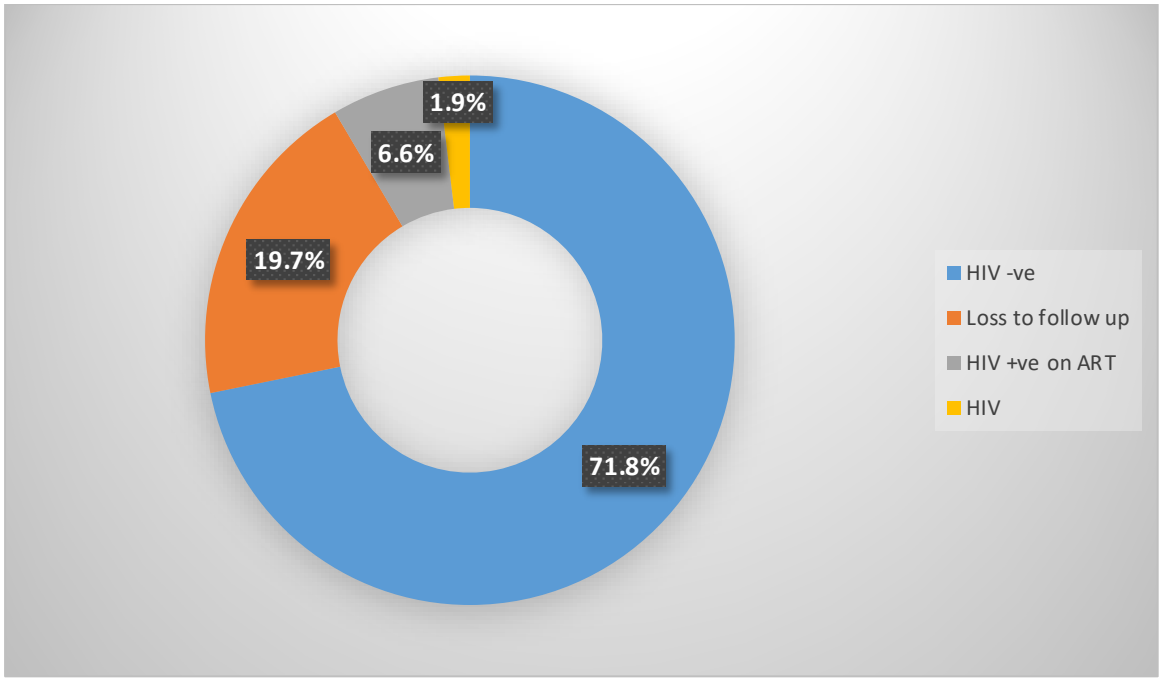

Figure 4: Overall status of the identified HIV exposed infants and children by 18 months of age at Kiambu Level V Hospital.

CHAPTER 5

5.1 DISCUSSION

The Kenyan National guidelines published in 2018 and in line with the WHO guidelines, dictates that early infant diagnosis of HIV in HIV exposed infant should be done at 6 weeks of age or 1st contact thereafter (14). According to our findings, 99.2% of HIV exposed infants had contact with a health care worker at 6 weeks of age during immunization coinciding with the appropriate age for early HIV diagnosis. Overall, 14.9% (54/362) of infants were identified as having missed opportunity for early diagnosis of HIV. This was lower as compared with a prospective study done by Udochisom CA et al in North-Central Nigeria in 2018 on missed opportunities for early diagnosis of HIV which showed that 27.8% of infants had missed opportunity for early diagnosis of HIV within 5 to 8 weeks of age and retrospective study done by N.A Phiri et al in Northern Malawi which showed that 50% of infants in both central and district hospital had missed opportunity for early diagnosis of HIV within 6-8 weeks of age (20)(22). A retrospective cohort study done in Kenya, by Douglas Gaitho et al between January 2015 and December 2017, showed a higher percentage of missed opportunity of 21% in early HIV diagnosis of HIV exposed infants within 2 months of age compared to 14.9% in our study (18).

Findings from this study showed that 10.5% of infants had a missed opportunity for the 2nd HIV DNA PCR test at 6 months, 15.3% for the 3rd HIV DNA PCR test at 12 months and 21.2% of children had a missed opportunity for the HIV antibody test at 18 months of age. These findings were lower when compared to a retrospective study done by Rogers Ankunda et al which reported loss to follow up of 28.7% at 6 months, 40.6% at 12 months and 48% at 18 months respectively (24).

According to our findings, entry point through the inpatient department/ward had a significant association with infant missing an opportunity for early diagnosis of HIV infection at 6 weeks of age. Those infants noted to have had their first HIV DNA PCR test at the age of more than 6 weeks were noted to have been referred from the inpatient ward and majority of the results turned out positive. Mother's duration on ART had a significant association with infant missing an opportunity for early HIV diagnosis. Those infants/ children whose mothers had been on ART, especially for a median of 12 months, were less likely to miss an opportunity for early HIV diagnosis compared to those infants/ children whose mothers were initiated on ART at same time infant was enrolled. This could be attributed to the fact that the mothers who had

been on ART before or during pregnancy had been educated by the health-care workers on early infant HIV DNA PCR testing done at 6 weeks of age and thus were aware. Mother's viral load count at time of infant/child enrolment was found to have a significant association with infant/child missing an opportunity for early HIV diagnosis. Those mothers who had viral load of less than 1000copies/ml were less likely to miss having their infant tested at 6 weeks of age compared to those mothers who had no viral load done. The sex of the infant, mother's age, mother's education level, mother's employment status, mother's ART regimen, mother's place of delivery and mother's marital status were not found to be significantly associated with infant/child missing an opportunity for early HIV diagnosis.

Our findings are similar to other studies. Bekana Kebede et al carried out a retrospective cohort study and identified certain predictors for early infant diagnosis: mother having prenatal care, mother having received ART during pregnancy and mother having delivered in a public facility. David Gaitho et al carried out a retrospective cross-sectional study and the factors associated with late age of at first HIV PCR test were: mothers who were not on ART at time of infant's HIV PCR test and infants who had not received ARV prophylaxis. Comparing these two studies with our findings, mothers ART duration was identified as being an important predictor for early HIV diagnosis in infants/children. According to our study, place of delivery was not identified as being an important predictor for early HIV diagnosis (17)(18).

At 6 weeks, the infant HIV infection rate was 2.9% of infants among the babies who accessed HIV DNA PCR testing. One third (33%), of all the HIV infected infants and children acquired HIV infection by 6 weeks of age. This proportion was higher when compared to a study done by David Gaitho et al which showed a positivity rate of 1.2% at first HIV DNA PCR test (18). Overall, mother to child HIV transmission (MTCT) rate was 10.5% of by 18 months of age. This proportion was higher when compared to a study done by Alamdo AG et al, carried out over the same period of time, and the results showed a MTCT rate of only 0.61% by 18 months of age (25). Twenty seven infants and children were identified as HIV positive but only 77.8% were started on treatment whereas 22.8% were not linked to care as five of them were lost to follow up and one died before linkage was done. This was lower when compared with a study done by NA Phiri et al in Northern Malawi which showed that 92% of HIV positive infants were started on treatment in the central hospital (22).

According to our findings, only 74% (222/300) of the children had all three HIV DNA PCR tests done (at 6 weeks, 6 months and 12 months respectively) and HIV antibody test done at 18 months of age. Overall, 21% missed all the four tests due to loss to follow up. The

percentage was lower when compared to the results obtained from study done by Alamdo AG et al which showed that 78.65% of infants had all the four tests done by 18 to 24 months of age (25).

5.2 STRENGTHS

1. Large sample size thus better representation of the population under study.
2. The findings of this study will be helpful information to the facility involved to scale up on early HIV diagnosis to allow for early commencement of antiretroviral therapy to reduce HIV related illnesses and death due to HIV in these children.

5.3 LIMITATIONS

1. This study was carried out in one health care delivery region in Kiambu County limiting the ability to generalize the results to the HIV exposed infants and children in Kiambu County.
2. This study did not interview the health care workers on factors associated with missed opportunities and this would have been important especially in those areas which referred few patients to the PMTCT clinic such as maternity, inpatient wards and outpatient department which referred patients more than 6 weeks of age.
3. Due to SARS COV2 infection and the restrictions that had been put into place, the PMTCT clinic and records department were closing earlier than usual thus limited time to collect data thus taking a bit of longer time to finish collecting data.

5.4 CONCLUSION

1. Prevalence of missed opportunities for early diagnosis of HIV (at 6 weeks of age) in HIV exposed infants 0-18 months at Kiambu Level V Hospital was low at 14.9% but could have been lower as 99.2% of infants had contact with health care worker at 6 weeks of age during immunization.
2. Factors that were associated with missed opportunities for early diagnosis of HIV were: entry point through the inpatient ward; mothers who ART was initiated at same time infant was enrolled (denoting diagnosis of HIV was made at that time) and mothers who had no viral load done at time of infant's enrolment which could have signified

that maternal HIV diagnosis was done at same time infant was enrolled thus no blood sample had been taken yet to measure the viral load.

3. The proportion of infants HIV infected by 6 weeks of age was high at 2.9% and this is the period that captures infections transmitted through pregnancy and delivery.
4. The proportion of HIV infected children 0-18 months of age who were started on ART was low at 77.8%.
5. The proportion of all HIV exposed children who had all three HIV DNA PCR tests done (at 6 weeks, 6 months and 12 months respectively) and HIV antibody test done at 18 months of age was low at 74%. Overall, 21% of the HIV exposed children did not have a final diagnosis, in terms of their HIV status, by end of 18 months due to loss to follow up.

5.5 RECOMMENDATIONS

5. To ensure that at infant's 6 week vaccination, both the mother and infant's HIV status should be known to avoid delay in early diagnosis of HIV.
6. All patients 0 to 18 months of age admitted in the ward should have a HIV test done as soon as possible to avoid missing any opportunity for early diagnosis and early initiation of treatment.
7. Development of strategies to ensure all HIV exposed infants/children have all four tests done by 18 months of age.
8. Qualitative study with staff at the facility should be considered in future studies to determine the challenges experienced in following guidelines and specifically making sure that no HIV exposed infant/child misses an opportunity for early diagnosis of HIV.

REFERENCES

1. Tindyebwa D, Kayita J, Musoke P, Eley B, Nduati R, Tumwesigye N, et al. Handbook on Paediatric AIDS in Africa by the African Network for the Care of Children Affected by HIV/AIDS-ANECCA Editors. 2017;187–207.
2. UNAIDS. Data 2020. Program HIV/AIDS [Internet]. 2020;1–248. Available from: https://www.unaids.org/en/resources/documents/2020/unaids-data%0Ahttp://www.unaids.org/sites/default/files/media_asset/20170720_Data_book_2017_en.pdf
3. MOH-NASCOP. Prevention of Mother to Child Transmission Downloads | Division of National AIDS & STI Control Program [Internet]. eMTCT framework 2016-2021. 2016 [cited 2021 Jun 22]. p. 1–8. Available from: https://www.nascop.or.ke/prevention-of-mother-to-child-transmission-downloads/
4. De Cock KM, Fowler MG, Mercier E, De Vincenzi I, Saba J, Hoff E, et al. Prevention of mother-to-child HIV transmission in resource-poor countries: Translating research into policy and practice. J Am Med Assoc. 2000;283(9):1175–82.
5. AVERT. Prevention of mother to child transmission of HIV [Internet]. 2019. Available from: https://www.avert.org/professionals/hiv-programming/prevention/prevention-mother-child
6. Yogev R, Gould Chadwick E. Chapter 276 - Acquired Immunodeficiency Syndrome (Human Immunodeficiency Virus). Nelson Textb Pediatr 2-Volume Set. 2016;1645-1666.e1.
7. UNAIDS. Start free Stay free AIDS free [Internet]. Start free Stay free AIDS free. 2020. Available from: https://www.unaids.org/en/resources/documents/2020/start-free-stay-free-aids-free-2020-progress-report
8. Abrams EJ, Wiener J, Carter R, Kuhn L, Palumbo P, Nesheim S, et al. Maternal health factors and early pediatric antiretroviral therapy influence the rate of perinatal HIV-1 disease progression in children. Aids. 2003;17(6):867–77.
9. John GC, Nduati RW, Mbori-Ngacha DA, Richardson BA, Panteleeff D, Mwatha A, et al. Correlates of Mother-to-Child Human Immunodeficiency Virus Type 1 (HIV-1) Transmission: Association with Maternal Plasma HIV-1 RNA Load, Genital HIV-1 DNA Shedding, and Breast Infections. J Infect Dis [Internet]. 2001 Jan 15;183(2):206–

12. Available from: https://academic.oup.com/jid/article/183/2/206/846601

10. Newell ML, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: A pooled analysis. Lancet. 2004;364(9441):1236–43.

11. Violari A, Cotton MF, Gibb DM, Babiker AG, Steyn J, Madhi SA, et al. Early Antiretroviral Therapy and Mortality among HIV-Infected Infants. N Engl J Med. 2008;359(21):2233–44.

12. Wamalwa D, Benki-Nugent S, Langat A, Tapia K, Ngugi E, Slyker JA, et al. Survival benefit of early infant antiretroviral therapy is compromised when diagnosis is delayed. Pediatr Infect Dis J [Internet]. 2012 Jul;31(7):729–31. Available from: /pmc/articles/PMC3756892/

13. Organization WH. Antiretroviral therapy for HIV Infection in Infants and children: Towards Universal Access HIV/AIDS Programme. Vol. 4911, World Health Organization. 2010.

14. Drugs A, Infection PHI V, Aids N, Program STIC. Kenyan guidelines on use of antiretroviral drugs for treating and preventing HIV infection in Kenya. 2018;10–3.

15. Zijenah LS, Moulton LH, Iliff P, Nathoo K, Munjoma MW, Mutasa K, et al. Timing of mother-to-child transmission of HIV-1 and infant mortality in the first 6 months of life in Harare, Zimbabwe. Aids. 2004;18(2):273–80.

16. Gm Makau, Fn Okwara, Jp Oyore. Determinants of early infant diagnosis and treatment of HIV among exposed infants in informal settlements in Nairobi, Kenya. East Cent Africa Med J. 2015;2:74–9.

17. Kebede B, Gebeyehu A, Jain S, Sun S, Haubrich R. Delay in Early Infant Diagnosis and High Loss to Follow-Up among Infant Born to HIV-Infected Women in Ethiopia. World J AIDS. 2014;04(04):402–12.

18. Gaitho D, Kinoti F, Mwaniki L, Kemunto D, Ogoti V, Njigua C, et al. Factors associated with the timely uptake of initial HIV virologic test among HIV-exposed infants attending clinics within a faith-based HIV program in Kenya; a cross-sectional study. BMC Public Health. 2021 Dec;21(1):1–7.

19. Goggin K, Wexler C, Nazir N, Staggs VS, Gautney B, Okoth V, et al. Predictors of Infant Age at Enrollment in Early Infant Diagnosis Services in Kenya. AIDS Behav.

2016;20(9):2141–50.

20. Anaba UC, Sam-Agudu NA, Ramadhani HO, Torbunde N, Abimiku A, Dakum P, et al. Missed opportunities for early infant diagnosis of HIV in rural North-Central Nigeria: A cascade analysis from the INSPIRE MoMent study. PLoS One. 2019;14(7).

21. Woldesenbet SA, Jackson D, Goga AE, Crowley S, Doherty T, Mogashoa MM, et al. Missed opportunities for early infant HIV diagnosis: Results of a national study in South Africa. J Acquir Immune Defic Syndr. 2015;68(3):e26–32.

22. Phiri NA, Lee H-Y, Chilenga L, Mtika C, Sinyiza F, Musopole O, et al. Early infant diagnosis and outcomes in HIV-exposed infants at a central and a district hospital, Northern Malawi. Public Heal Action. 2017;7(2):83–9.

23. Mwanamkasi T. prevalence and factors associated with missed opportunities for HIV testing and diagnosis of children accessing health care services at Mbagathi District Hospital. 2017.

24. Ankunda R, Cumber SN, Atuhaire C, Kabanda T, Nkfusai CN, Wirsiy FS, et al. Loss to follow-up and associated maternal factors among HIV-exposed infants at the Mbarara Regional Referral Hospital, Uganda: A retrospective study. BMC Infect Dis. 2020 Mar 19;20(1):1–9.

25. Alamdo AG, King EJ. Retention in care and health outcomes of hiv-exposed infants in a prevention of mother-to-child transmission of hiv (Pmtct) cohort in addis ababa, ethiopia. HIV/AIDS - Res Palliat Care. 2021 Feb 10;13:171–9.

APPENDICES

APPENDIX 1: STANDARD TOOL FOR DATA ABSTRACTION

Table 1: Characteristics of the children

Variable	**Frequency (%)**
Median age of the child at enrolment (IQR) in weeks	
Sex of the infant Male Female	
Entry point 1.Ward/IPD 2. OPD 3. Maternity 4. CCC 5. MCH/PMTCT 6. Transfer in	
Feeding option Exclusive BF Not BF	
Place of delivery Facility Home	
ARV prophylaxis regimen NVP during BF + AZT for 6 weeks NVP for 12 weeks + AZT for 6 weeks NVP for 12 weeks	

NVP for 6 weeks NVP for 6 weeks + AZT for 6 weeks Single dose NVP Only NVP during BF None	
Immunization Up to date Loss to follow up Not documented	

Table 1: Maternal socio-demographic and clinical characteristics

Variable	**Frequency (%)**
Mother's age, mean (SD) in years	
Mother's education level None Primary Secondary Tertiary	
Mother's employment status Formal employment Self-employment Informal employment	

None	
Marital status Married Single Divorced Widowed Cohabiting	
Mother's duration on ART in months Median (IQR) Min-Max	
Mother's VL at child enrolment <1000 >=1000 Not done	
Mother's ART regimen First line Second line	
Place of delivery Facility Home	

Table 2: Infant's HIV DNA PCR testing

Variable	Frequency (%)	95% CI
At 6 weeks Done Missed		
At 6 months Done Missed		
At 12 months Done Missed		
At 18 months Done Missed		

Table 3: Missed opportunities at 6 weeks and the associated factors

Variable	**Missed**	**Did not miss**	**OR (95% CI)**	**P value**
Sex Male Female				
Entry point MCH/PMTCT Ward/IPD				

OPD Maternity CCC Transfer in				
Mother's age, mean (SD)				
Mother's education level None Primary Secondary Tertiary				
Mother's employment status Formal employment Self-employment Informal employment None				
Mother's duration on ART, median (IQR) in months				
Mother's VL at child enrolment <1000 >=1000 Not done				
Mother's ART regimen First line Second line				

Table 4: HIV infection and linkage to treatment

Variable	Frequency (%)
PCR results at 6 weeks	
HIV-infected	
HIV negative	
PCR results at 6 months	
HIV-infected	
HIV negative	
PCR results at 12 months	
HIV-infected	
HIV negative	
PCR results at 18 months	
HIV-infected	
HIV negative	
Final results by 18 months of age	
HIV-infected	
HIV negative	
Unknown	
MTCT rate	
HIV-infected	
HIV negative	
Linkage to treatment	
Started ART	
Not linked	

APPENDIX 2: WAIVER OF INFORMED CONSENT

Date:

Study title: MISSED OPPORTUNITIES FOR DIAGNOSIS OF HIV IN HIV EXPOSED INFANTS AND CHILDREN 0-18 MONTHS AT KIAMBU LEVEL V HOSPITAL.

Investigator: Dr Betty Mburu (MBChB- University of Nairobi)

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We are doing this study to determine the missed opportunities for diagnosis of HIV in HIV exposed infants and children 0-18 months at Kiambu level V Hospital.

Introduction:

HIV AIDS is a major cause of infant and childhood mortality and morbidity in Africa. Mother to child transmission of HIV (either through pregnancy, during delivery or through breastfeeding) accounts for >95% of childhood paediatric infections. Early diagnosis of HIV

infection and early initiation of antiretroviral therapy reduces death rate by 76% and HIV disease progression by 75% during infancy. Without treatment, 35.2% of HIV infected infants will have died by 1 year of age and 52.5% by age of 2 years. WHO recommends early infant diagnosis of HIV to be done at 4-6 weeks of age as during this period majority of infections acquired during pregnancy and during delivery can be identified. In Kenya, 94% of HIV-infected pregnant women were accessing treatment in 2019. Early infant diagnosis by 8 weeks of age was 68.8% compared with 67.1% in 2010. Between year 2017 and 2019, 450 HIV exposed infants were attended to at Kiambu Level V hospital. According to the Kenyan National guidelines, all HIV exposed infants should have their first HIV DNA PCR test done at 6 weeks or first contact thereafter but less than 90% have it done at 6 weeks in Kiambu Level V hospital despite very good immunization coverage at that age. Also less than 90% of the HIV infected infants/children are started on treatment. This data signifies a gap in early infant diagnosis of HIV and early initiation of treatment. It is important to diagnose HIV infection in children at the earliest time possible at least by 6- 8 weeks of age to allow for early commencement of treatment which improves survival. Early initiation of antiretroviral therapy by 12 weeks reduces HIV related illnesses by 76% and death by 75%. Kenya has come up with guidelines on early infant and children (0-18months) diagnosis of HIV to ensure no infant/child is missed out on diagnosis of HIV infection and early commencement of treatment

Benefits:

The study is a retrospective study and we are requesting for a waiver of informed consent in order to be able to get the information necessary for the study.

Practicality:

It will not be possible to do this research without a waiver of informed consent because we are analysing already documented data prior to the time of collection of data and getting informed consent of the subjects is not feasible either from the fact that the contact information may be missing, have changed and the subject may live too far from the site of the study.

Risk:

The research will pause no risk to the patient as we will not come into contact with them. The waiver of informed consent will be used to collect data already documented. Coding of data will be used to prevent the primary risk that is breach of confidentiality.

Confidentiality

Rights and welfare of the subjects be respected by abstracting identifiable personal data and omitting unnecessary data. This will furthermore prevent any breach of confidentiality.

Problem/Question:

If any problem or question about the study, you can contact the principal investigator, **Dr Betty Mburu** Tel no. +254725578570.

If any enquiry on the rights and ethical consideration about this study, you can contact the **Kenyatta National Hospital- University of Nairobi Ethics and Research Committee (KNH-UON ERC)** Tel no. 276300 Ext 44355.

Investigator's Signature: _____

Date: _____

APPENDIX 3: ETHICAL APPROVAL

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13th August 2020

Dr. Betty Mburu
Reg. No.H58/11417/ 2018
Dept.of Paediatrics and Child Health
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Mburu

RESEARCH PROPOSAL –MISSED OPPORTUNITIES FOR EARLY DIAGNOSIS OF HIV IN HIV EXPOSED INFANTS AND CHILDREN 0-18 MONTHS AT KIAMBU LEVEL V HOSPITAL (P228/04/2020)

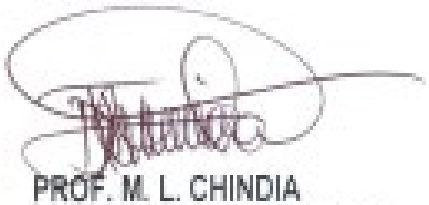
This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and approved your above research proposal. The approval period is 13th August 2020 – 12th August 2021.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC websitehttp://www.erc.uonbi.ac.ke

Yours sincerely,



PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

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The Senior Director, CS, KNH
The Chairperson, KNH- UoN ERC
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