

Prevention of mother-to-child transmission of HIV at
Kasangati Health Centre, Uganda

Degree project

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1. Abstract

Prevention of mother-to-child transmission of HIV at Kasangati Health Centre, Uganda

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Introduction: More than 90% of children living with HIV acquire the infection via MTCT (mother-to-child transmission) during pregnancy, birth, or breastfeeding. Without treatment, half of them will die before their second birthday. In Uganda, there has been large focus on PMTCT (prevention of mother-to-child transmission), but postnatal follow-up has been insufficient. Only 1/3 of infants received immediate diagnosis of HIV in 2015, and in 2016, only 43% of HIV-positive children had access to treatment in Uganda.

Aims: To study the postnatal follow-up of children born by women living with HIV at KHC (Kasangati Health Centre).

Methods: A descriptive cross-sectional study was conducted through interviews using a questionnaire based on WHO guidelines. The study population consisted of 103 mothers living with HIV whose youngest child was between six weeks and 18 months old and who were visiting the antenatal or the HIV clinic at KHC.

Results: Only one of the children (1%) had acquired HIV. Regarding consistency with guidelines, 80% of the babies had received recommended infant prophylaxis, nevirapine for six to twelve weeks. At six weeks of age, 84% of the babies had been tested for HIV. Only 43% had been tested six weeks after cessation of breastfeeding. At 18 months of age, 57% had been tested.

Conclusions: WHO guidelines are being followed to a large extent at KHC, which could possibly explain the low rate of MTCT (1%) that was found, a transmission rate nearly as low as in high-resource countries such as Sweden (0.5%) despite having limited resources and a high prevalence of HIV.

Key words: HIV, PMTCT, prevention, pregnancy, resource-limited settings

2. Abbreviations

3TC	lamivudine
AAAQ	availability, accessibility, acceptability, quality
AIDS	acquired immunodeficiency syndrome
ART	antiretroviral treatment
CD4	cluster of differentiation 4
CCR5	chemokine receptor 5
CTX	co-trimoxazole
EFV	efavirenz
FTC	emtricitabine
GDP	gross domestic product
GNI	gross national income
HIV	human immunodeficiency virus
KHC	Kasangati Health Centre IV
MTCT	mother-to-child transmission
NVP	nevirapine
PCR	polymerase chain reaction
PMTCT	prevention of mother-to-child transmission
RNA	ribonucleic acid
TDF	tenofovir disoproxil fumarate
UDHS	Uganda Demographic and Health Survey
UNAIDS	the joint United Nations programme on HIV/AIDS
WHO	World Health Organization
ZDV	zidovudine

3. Background

3.1 Global burden of HIV

Communicable, or infectious, diseases are a major global health issue causing more than 7.1 million deaths in 2015. While accounting for a fraction of deaths in high-income countries, communicable diseases together with maternal causes (conditions arising during pregnancy and childbirth) and nutritional deficiencies account for the majority of deaths in low-income countries (1).

One of the leading causes of morbidity and mortality among communicable diseases is HIV (human immunodeficiency virus) and its consequence AIDS (acquired immunodeficiency syndrome). AIDS was first recognized in 1981 in the United States when young and healthy homosexual men were suddenly acquiring rare infections and dying. It was found that the affected had severe immunodeficiency and lack of treatment lead to high morbidity and mortality (2). A few years later, the causative agent HIV was discovered and later that it originated from central Africa (3). Soon, the number of new cases increased rapidly and HIV became a pandemic, an outbreak in most of the countries in the world (4). After years of hopelessness and struggle, the first antiretroviral drugs were introduced in 1987, and it took until 1996 to find effective medicine when combination ART (antiretroviral therapy) revolutionized the field (2). Even though the treatment is not curative, people living with HIV who are receiving treatment have little effect on life expectancy (5).

Since then, HIV incidence and mortality has declined rapidly. It reached its peak incidence in 1997 with 2.8 million new cases and in 2005, the highest yearly mortality with 1.7 million deaths caused by AIDS (6), see Fig. 1. The numbers have decreased and in 2016, 2.1 million people were newly infected and 1.1 million deaths were caused by HIV, whereas the

prevalence had increased to 36.7 million due to an accumulation of new infections together with prolonged life-expectancy (7).

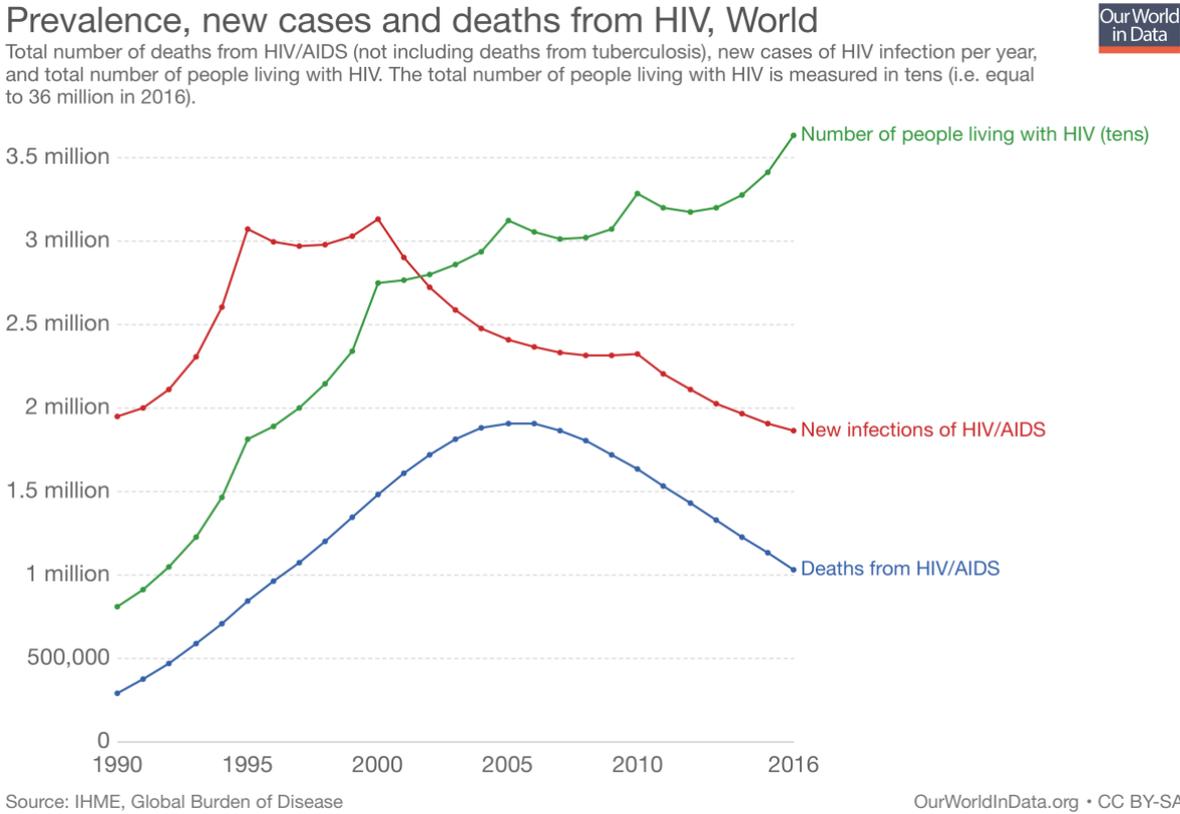


Figure 1. Showing the global trends in prevalence, incidence and death rates caused by HIV/AIDS, the peaks and how incidence and death rates are decreasing. The prevalence numbers are ten times higher than the scale at the y-axis. Taken from ourworldindata.org.

Despite the success, many challenges still remain, mostly in resource-limited settings that are more affected than others. Eastern and southern Africa with 6% of the world's population, is home to more than half of the people living with HIV (8). A vulnerable group in this setting is HIV-exposed infants, infants born to women living with HIV. WHO (World Health Organisation) has established a vision stating that zero infants should be born with HIV, as a key point in ending the HIV pandemic. Every day, however, 400 children below 15 years of age were infected with HIV (9) and more than 90% of them acquired the infection from their

mothers in 2015 (10). The consequence of not treating infected infants is devastating, 50% will die before two years of age (11). It is therefore important not only to prevent transmission but also to early identify infants who are infected with HIV and treat them immediately. If the management and follow-up of HIV-exposed infants can be improved, the morbidity and mortality will decrease, and we will be one step closer to a future with an AIDS-free generation.

3.2 HIV and PMTCT in Uganda

Uganda is an East African country located in Sub-Saharan Africa with an area of 241,551 km² (12) and a population of 41.5 million people in 2016. In 2015, the GNI (gross national income) per capita was 1820 USD and in 2014, the health expenditure was 7% of GDP (gross domestic product) (13). However, in 2013-2014, more than 40% of the health expenditure was paid out of pocket and government spending on health was only 1.4% of GDP (14). The life expectancy at birth (2015-2020) is 60 years (13).

Uganda is one of the countries that has been most affected by HIV. In 2016, 1.4 million people were living with HIV, 52,000 were newly infected and 28,000 deaths were caused by AIDS (15). The country has a young population, 48% were below 15 years of age in 2014 (12), which could lead to current and future risks of transmission, both sexual and through MTCT (mother-to-child transmission).

Early in the HIV epidemic it was discovered that MTCT could occur during pregnancy, birth, and breastfeeding. A randomized, double-blind, placebo-controlled study in 1994 examined the effects of treating pregnant women that had not received ART during their pregnancies and their babies with ZDV (zidovudine). In the group that was given treatment, the relative

risk reduction of transmission to the baby was 68% (16). The insight that preventive measures can reduce the risk of infecting the babies substantially was the start of PMTCT (prevention of mother-to-child transmission). If no measures are taken, the risk of infants acquiring HIV are between 15 and 40% (17). If the mother is on ART and the baby is treated with infant prophylaxis the risk can be below 1%, which has been seen in resource-rich settings (18).

There has been large focus on PMTCT in Uganda. In 2011, UNAIDS (joint United Nations programme on HIV/AIDS) started the Global Plan to prevent HIV infections in 21 priority countries with the highest burden, where nearly 90% of pregnant women with HIV were living in 2009. Uganda reduced the number of infections by 86% between 2011 and 2015. An important part was to suppress the mothers' viral load, to lower the risk of transmission to the babies. In 2016, an estimated number of more than 95% of pregnant women living with HIV in Uganda were on ART (11). However, when it comes to postnatal follow-up, the progress has been insufficient. In 2016, 4,600 children were newly infected but only 47% of them were on treatment (15) and in 2015, no more than 1/3 received early infant diagnosis (a virological test before two months of age) (11).

3.3 Pathophysiology

Transmission of HIV occurs through contact with body fluids of an infected person via vaginal, anal, and oral sex, sharing needles when abusing intravenous drugs, blood transfusions, skin penetration injuries in healthcare workers, and MTCT during pregnancy, birth, or breastfeeding (19). Globally, sexual transmission is the most common followed by MTCT.

HIV can be transmitted to the baby prepartum (in utero), intrapartum (during birth), or postpartum (during breastfeeding). The most important risk factor for transmission is a high viral load in the mother's blood (20). Transmissions mostly occur through contact of the mother's infected body fluids, such as blood, vaginal secretions, and breast milk, with the child's mucus membranes in the gastrointestinal or nasopharyngeal tracts (21) where susceptible target cells, T cells expressing CD4 (cluster of differentiation 4) and CCR5 chemokine receptor 5), have been found (22). HIV can infect cells in the epithelial layer or by crossing the mucus membrane, via tears in the membrane or transcytosis (transport through the cells) (23). Both free virus and cells infected with virus are involved in the transmission (21).

Antepartum transmission is the least common route of transmission. If the mother is not breastfeeding, around 30% of transmissions occur antepartum and 70% intrapartum (20). Most of the antepartum transmissions occur during the third trimester, only a few percent during the second trimester and even fewer during the first trimester. The placenta is an effective barrier and allows few infections (21). However, in vitro studies have shown that HIV may infect and cross placental cells, trophoblasts, which indicates that target cells could be reached, and the foetus could therefore be infected (24).

A more significant route is intrapartum transmission (21). During contractions, the barrier between maternal and infant blood can be disrupted, and placental microtransfusions, mixing of maternal and foetal blood, can occur (25). Another route is oral infection, when the infant swallows vaginal fluids that get in contact with its' mucus membranes (21). Delivering the baby by caesarean section reduces the transmission rate with approximately 50% in non-treated women but no risk reduction is seen in well-treated women. However, caesarean

sections increase the risk of severe complications such as haemorrhage, infections, uterine ruptures, and placenta accreta, why vaginal deliveries are recommended for well-treated women (26).

Postpartum transmission is a significant route, due to long and frequent periods of contact between breast milk and the child's gastrointestinal tract (27). The risk of transmission if the mother is breastfeeding is an additional 14% (28) and it has been shown that breastfeeding causes more than 40% of infant HIV infections (29).

3.4 WHO guidelines on postnatal PMTCT

To prevent mother-to-child transmission of HIV, WHO has established guidelines on ART for pregnant and breastfeeding women, infant prophylaxis, infant feeding, and testing that are implemented in national guidelines. For a summary of WHO guidelines on postnatal follow-up of children born by women living with HIV in resource-limited settings, see Fig. 2.

3.4.1 Antiretroviral treatment

WHO recommends lifelong ART for all people living with HIV at any CD4 count, regardless of clinical stage of disease. The previous recommendation was to offer treatment only during pregnancy and breastfeeding. The advantage of lifelong ART is that it improves the mother's health, reduces the risk of transmission in future pregnancies and has a potential to reduce the risk of transmission to a sexual partner (30). Some studies have shown that women on lifelong treatment are less likely to be lost to follow-up postpartum (31). It has also been shown that lifelong ART is more cost-efficient and increases quality of life in both mothers and their children (32).

When initiating treatment in patients who have not been treated before, a fixed-dose combination containing three drugs is used; TDF (tenofovir disoproxil fumarate), EFV (efavirenz), and 3TC (lamivudine) or FTC (emtricitabine) (33).

3.4.2 Infant prophylaxis

All HIV-exposed infants are recommended prophylaxis with antiretroviral drugs during the first period of life. The choice of treatment differs depending on if the infant is breastfed or not and if the infant is considered to be at high or low risk of acquiring HIV.

High-risk infants are those with mothers living with HIV who have been on ART for less than four weeks at birth, who had a high viral load (> 1000 copies of HIV RNA (ribonucleic acid) per millilitre of blood) four weeks before birth, who got infected during pregnancy or breastfeeding, or those who were first diagnosed with HIV during the postpartum period. All high-risk infants should receive daily ZDV and NVP (nevirapine) for six weeks. If they are breastfed, the treatment should be extended for six more weeks (twelve weeks in total) with ZDV and NVP or NVP only (34).

Infants who are considered to be at low risk and are breastfed should be treated with daily NVP for six weeks. Low-risk infants who are receiving replacement feeding should be treated with daily NVP or twice-daily ZDV for four to six weeks.

In addition, CTX (co-trimoxazole), a fixed-dose combination of two antibiotics, sulfamethoxazole and trimethoprim, is recommended as prophylaxis in resource-limited settings to prevent coinfections such as malaria and *Pneumocystis jirovecii* pneumonia. Infants should be treated with CTX from four to six weeks of age until there is no risk of

acquiring HIV, which is determined by age-appropriate testing after cessation of breastfeeding (35).

3.4.3 Infant feeding

The purpose of the recommendations on breastfeeding is to achieve the greatest likelihood of HIV-free survival among HIV-exposed infants, either with or without breastfeeding. In countries with high prevalence of HIV and where pneumonia, diarrhoea, and undernutrition are common causes of ill-health and death, the benefits of protecting the infant from getting these diseases outweigh the risk of acquiring HIV through breastfeeding. National recommendations are based on which approach will give the greatest chance of HIV-free survival. The following guidelines are intended for countries where breastfeeding is recommended, as in Uganda.

Mothers with HIV who are receiving ART and who have no sign of clinical, immune, or viral failure should breastfeed for 12-24 months or longer. During that time, they should have full support for ART adherence. Exclusive breastfeeding should last for six months and after that, complementary foods should be initiated. Breastfeeding should continue until a safe diet containing all necessary nutrients can be given.

WHO recommends initiating breastfeeding in the first hour of life and breastfeeding on demand, when the infant wants to breastfeed. Even if the mother is not on ART, breastfeeding is recommended as the method to increase survival (36).

3.4.4 Testing

Serological and virological tests are used to diagnose HIV. Serological tests detect HIV antibodies, newer serological combination tests detect HIV antibodies and HIV antigen and virological tests detect viral RNA. Testing of children younger than 18 months of age differs from testing of adults and older children. HIV-exposed infants have maternal antibodies against HIV that have crossed the placenta during pregnancy that can persist in the infants' blood up to 18 months. Therefore, serological tests can be positive even if the infant is uninfected, whereas this problem is avoided by using virological tests. Thus, it is recommended that all infants have virological testing at four to six weeks of age.

At approximately nine months of age, all infants should have a serological test. If the test is positive, a complementary virological test should be done. The definite diagnosis is determined when there is no more risk of acquiring HIV through MTCT. A final serological test is recommended when the child is 18 months old and has stopped breastfeeding at least six weeks earlier. A negative test excludes HIV infection.

All infants with signs or symptoms of HIV should be serologically tested. If the test is positive, a complementary virological test should be done.

If any virological test is positive, ART should be initiated immediately. A confirmatory virological test should be taken, but treatment should not be delayed while waiting for the second result (34, 37).

The recommendations on PMTCT from Uganda Ministry of Health are in accordance with the WHO recommendations mentioned above. Differences are that FTC is not included in the

first-line regimen when it comes to ART and that infant prophylaxis is only NVP, for six weeks if the infant has low risk of acquiring HIV and twelve weeks if the risk is high. The difference regarding breastfeeding is that the mothers are recommended to stop when the baby is twelve months old (38).

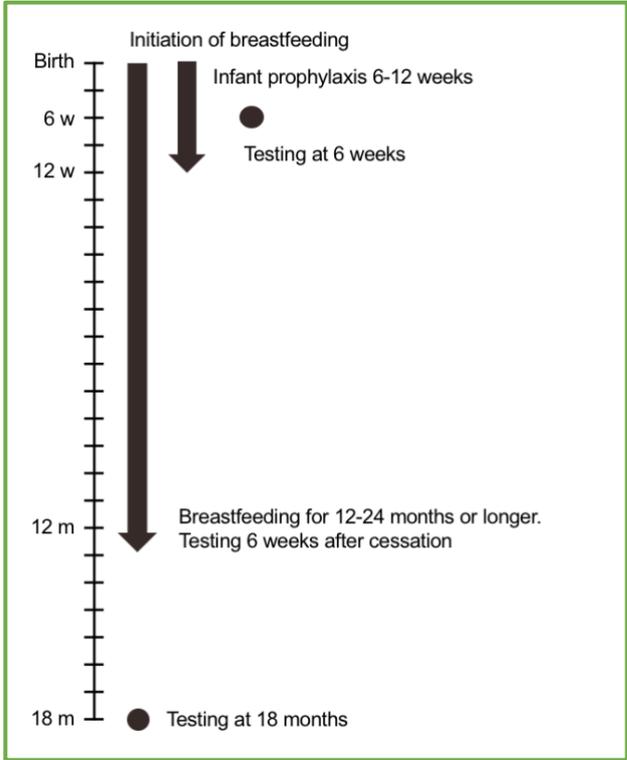


Figure 2. WHO guidelines on postnatal follow-up of children born by women living with HIV in resource-limited settings plotted in a timeline from birth to 18 months of age.

Exclusive breastfeeding is recommended for six months followed by mixed feeding for as long as it is needed. Treating the babies with infant prophylaxis for six to twelve weeks is recommended. Testing the babies for HIV is recommended at six weeks of age, six weeks after cessation of breastfeeding and at 18 months of age.

3.5 Wakiso District and Kasangati Health Centre

KHC (Kasangati Health Centre) is a type IV health centre, which means that it is the highest level of primary health care offering outpatient care, inpatient care, maternity and childcare

including deliveries and surgeries such as caesarean sections. It is located in the town Kasangati in Wakiso District, the district in Uganda with the largest population, 1.9 million people (39). The areas in Wakiso District are peri-urban and rural.

They follow Uganda National Guidelines but are limited by the lack of resources. Since it is a government health facility, health care is free, but materials are often out of stock. HIV care is prioritized, and ART is usually available.

There is strong focus on PMTCT at KHC. All pregnant mothers are tested for HIV, and if the results are positive, ART is initiated. After birth, they have services for mother-baby pairs until the baby is 18 months old. All HIV-exposed infants are given NVP syrup (oral suspension) for six to twelve weeks. If the syrup is out of stock, NVP pills are given. After that, they are treated with CTX until there is no risk of acquiring HIV through MTCT.

Virological testing is done at six weeks of age and six weeks after cessation of breastfeeding. They take capillary whole blood samples by a finger-stick with a lancet and drop it on a filter paper and let it dry. The dried blood sample is sent to a validated laboratory, Central Public Health Laboratories, to be analysed with PCR (polymerase chain reaction) to detect levels of HIV RNA. The test results return to KHC in two to four weeks.

Finally, they are serologically tested at 18 months of age. A capillary rapid diagnostic test is done and analysed immediately. If the children acquire HIV, lifelong follow-up continues at the HIV clinic.

4. Aim

The main purposes of this project were to study the postnatal follow-up of children born by women living with HIV at KHC and to determine if any areas for improvement could be found to further decrease MTCT of HIV in this area of Uganda.

The scientific issues were to determine:

- To what extent KHC was following WHO guidelines on:
 - Testing of babies; before six weeks of age, six weeks after cessation of breastfeeding, at 18 months of age, or if they present symptoms suggesting HIV infection.
 - Treating the babies with infant prophylaxis.
 - Initiating ART immediately in HIV-positive babies.
- The mothers' knowledge about HIV transmission and protection from transmission.
- The mothers' adherence to ART during pregnancy and after delivery.

5. Method

5.1 Study design and setting

The study is a descriptive cross-sectional study conducted through interviews using questionnaires at KHC in Kampala, Uganda, during seven weeks between February and April 2018.

5.2 Study population

The study population consisted of HIV-positive mothers. The inclusion criteria were mothers 18 years or older, who were diagnosed with HIV before or during pregnancy or at birth, and who had a child that was between six weeks and three years old. No exclusion criteria were formed.

5.3 Data collection

A semi-structured questionnaire with close-ended and multiple response questions was constructed. The general questions regarding HIV, adherence, and sociodemographic factors were collected from validated questionnaires from WHO and AIDS Clinical Trials Group (40). The other questions were based on WHO guidelines. The questionnaire was initially tested on 10 patients and some questions were revised after that.

Participants were included from the antenatal clinic two days a week and from the HIV clinic one day a week. HIV-positive mothers have follow-up at the antenatal clinic until 18 months after delivery and are then referred to the HIV clinic.

All patients having their regular appointments at the clinics, around 1050-1750 mothers, were considered for inclusion. They were informed about the study and approached us one by one

throughout the day. A total of 112 patients were directly asked to participate in the study. Only one patient declined because of lack of time. Interviews were done with 111 mothers. Five were later excluded because they were diagnosed with HIV when their child was a couple of months old and three were excluded because the baby was younger than six weeks old.

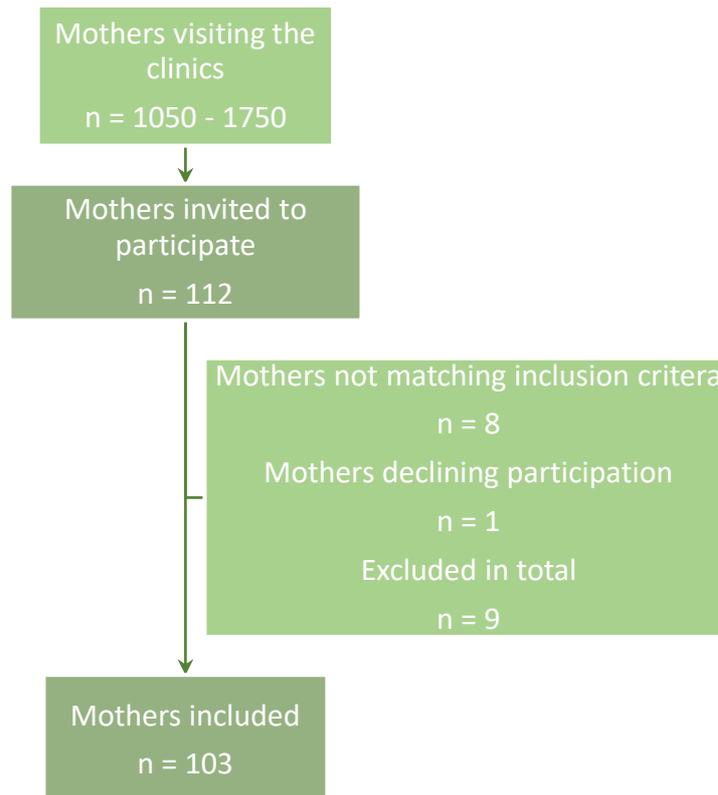


Figure 1. Flowchart describing the inclusion process. Around 1050-1750 mothers were visiting the clinics. A total of 112 mothers were asked to participate in the study. One mother declined and eight were later excluded because they did not match inclusion criteria. A final number of 103 mothers were included in the study.

The interviews were performed when the patients were waiting for their appointments outside the clinics and did not interfere in the health care they were given. A nurse working at the

ward at the health centre, who was not involved in the participants' care, was used to interpret between Luganda, the local language spoken in the area, and English. The same interpreter was used throughout the study. Before conducting the interviews, participants were given detailed information about the study and had the opportunity to ask questions. The majority of the interviews were performed in private, but due to lack of space, some of them were performed where they could be overheard by others. The interviews lasted for approximately 15-20 minutes.

Information about the mothers' CD4 counts and viral loads was planned to be collected, but this turned out to be impossible because the data collection was done without access to their medical records. The mothers did not have this information and it could not be found in the medical books they brought with them.

5.4 Statistical analysis

The data was analysed in SPSS Statistics. Comparisons between the groups was done using the Chi-square test and when sampling size was < 5 in any of the cells, Fisher's exact test was used. A p-value of < 0.05 was used to represent a significant difference.

6. Ethical considerations

Ethical permission was obtained from Dr. Ivan Nyenje, Medical Officer at KHC, before starting the data collection. Later, 2018-03-10, a written ethical permission was obtained from the Wakiso District Local Government. Informed verbal consent was acquired from all participants prior to the interviews. The mothers were informed that the study was completely voluntary and that they could stop at any time or decide to not answer all questions without giving a reason. No identity data was collected. If the mothers chose to participate or not had no impact on the health care they were given. Possible risks associated with participation in the study were minimal. In case of emotional distress, they had an opportunity to discuss it with the interpreting nurse. Although there were no direct benefits for the participants, the results could be helpful for women living with HIV and their children in the future.

7. Results

7.1 HIV diagnosis

The majority (89%) of the participants were receiving health care at the antenatal clinic, whereas 11% were at the HIV clinic.

All participants were on ART at the time of the interview. Most of them (76%) started treatment the same day they were diagnosed, see Fig. 1. Three percent waited one month before starting treatment, 3% waited two months, 8% waited between three and twelve months, and 4% waited more than twelve months with a maximum of three years and nine months. Six percent could not remember how long they waited before starting ART.

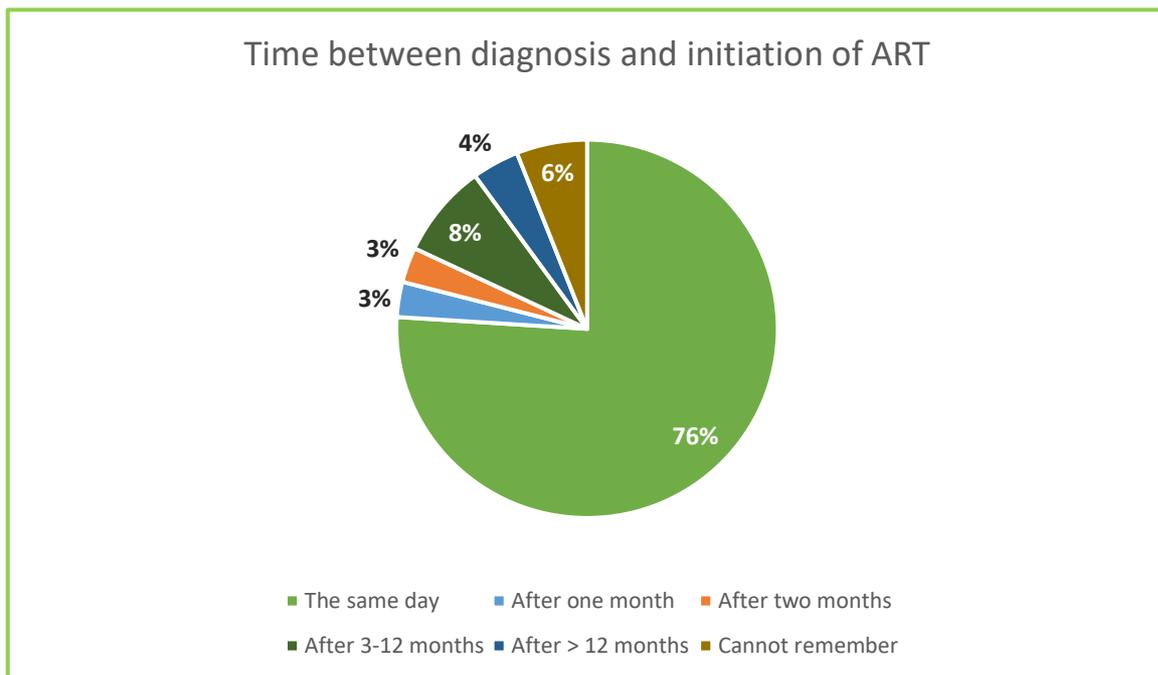


Figure 1. Time between when the mothers received their HIV diagnosis and when they initiated ART based on the question “When did you first start taking ART?”.

7.2 Knowledge about HIV transmission

The mothers' knowledge about HIV transmission was high regarding vaginal sex (95%) and sharing sharp instruments (62%), see Fig. 2. Regarding MTCT, their knowledge was poor (23%).

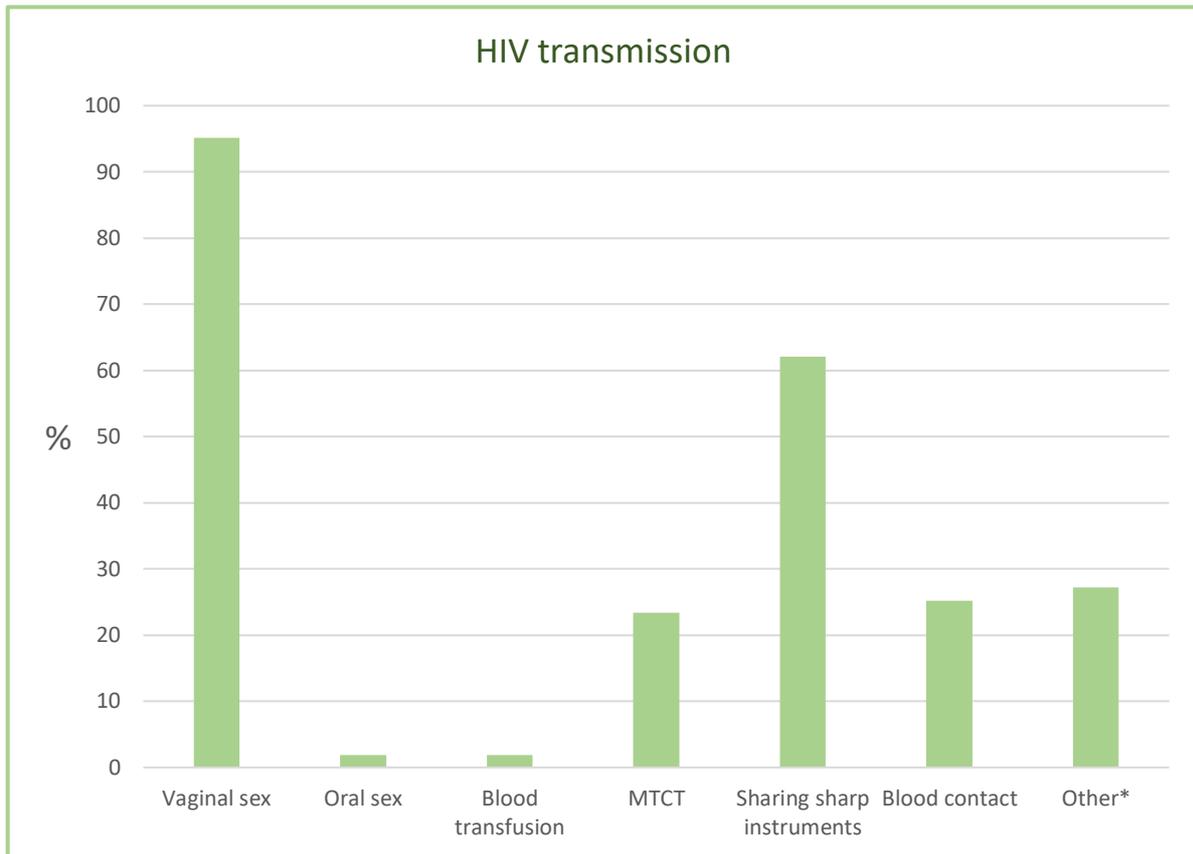


Figure 2. The mothers' knowledge about HIV transmission based on the question "What are some of the ways HIV can be transmitted?". * = Accidents, wounds, kissing, having many sexual partners, not being adherent to ART, forced sex, and sharing sponges.

The mothers' knowledge about protection was high regarding usage of condoms (83%), see Fig. 3. Only 19% knew that being adherent to ART as a way of protecting oneself. Other ways were abstaining from sex (10%) or reducing the number of partners (8%).

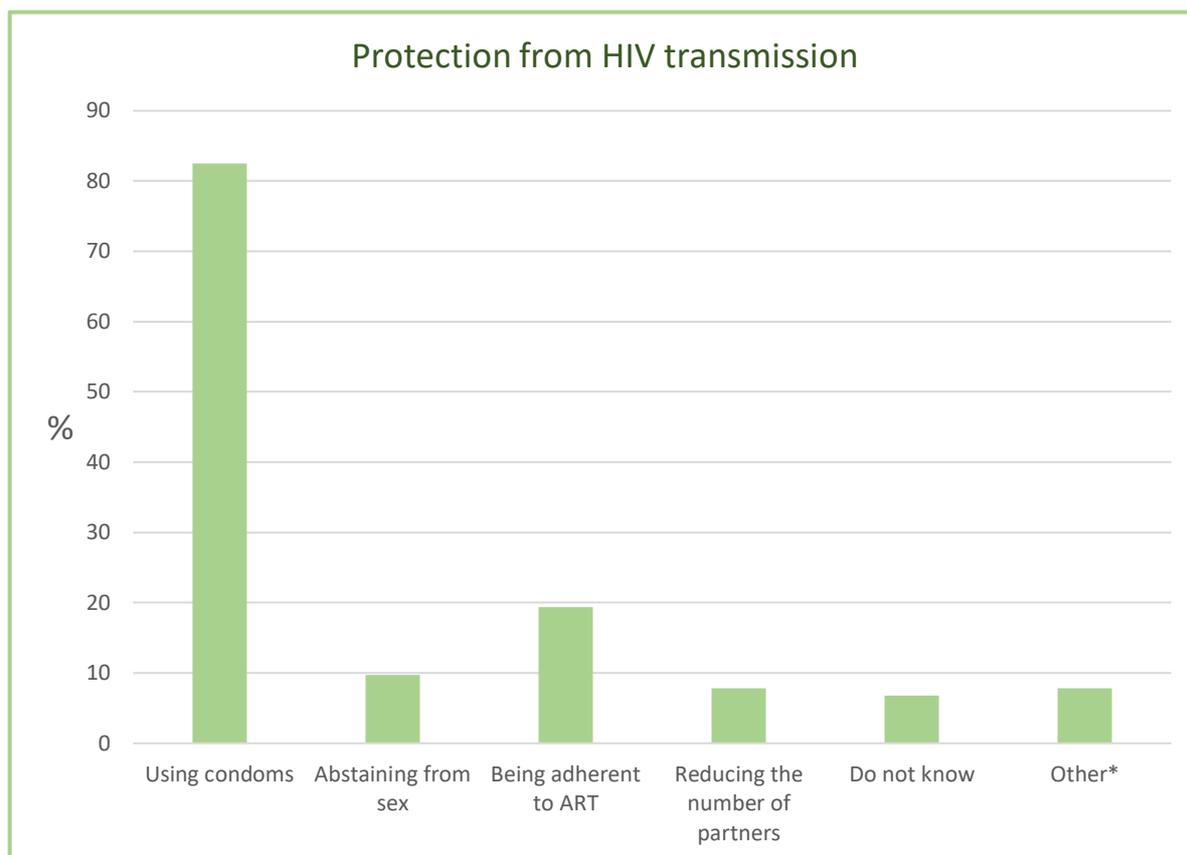


Figure 3. The mothers’ knowledge about protection from HIV transmission based on the question “What are some ways that an HIV-positive person can reduce the risk of transmitting the virus to another person through sexual contact?”. * = Avoiding sharp instruments, using female condoms, getting tested, if you have enough vaginal fluids.

7.3 Children, pregnancies, and adherence to ART

The number of children the participants had varied between one and eight (mean 3, median 2). The majority of mothers (89%) had between one and four children, 19% of the mothers had lost a child, 7% had lost two children, and 1% had lost three children.

The mothers’ treatments are presented in Table 1. All but two participants were on treatment during the pregnancy. Almost all (94%) continued with the same treatment after their baby was born, 6% changed treatment, but no one stopped taking treatment.

Table 1. The mothers' ART during pregnancy; if they were on treatment or not, if they knew the name of the drugs they were taking and if they were diagnosed with HIV during pregnancy. Multiple responses were possible.

Were you on ART during pregnancy?		N (% of cases)
Yes	TDF/3TC/EFV	12 (12)
	TDF/3TC/NVP	1 (1)
	NVP + EFV	1 (1)
	NVP	1 (1)
Yes, unknown treatment		86 (84)
No		2 (2)
Diagnosed during pregnancy		50 (49)
Total		153 (150)

The mothers' adherence to ART is shown in Fig. 4. Among mothers who were on ART during the pregnancy, 21% missed to take at least one dose at some time during the pregnancy. Most of them (16 out of 21) missed to take their medicine once, twice or three times, but five mothers missed more often than that.

During the first year after their baby was born, 15% missed to take their medicine. The majority (11 out of 15) missed to take a dose once, twice or three times, but four mothers missed more often than that or for one whole week.

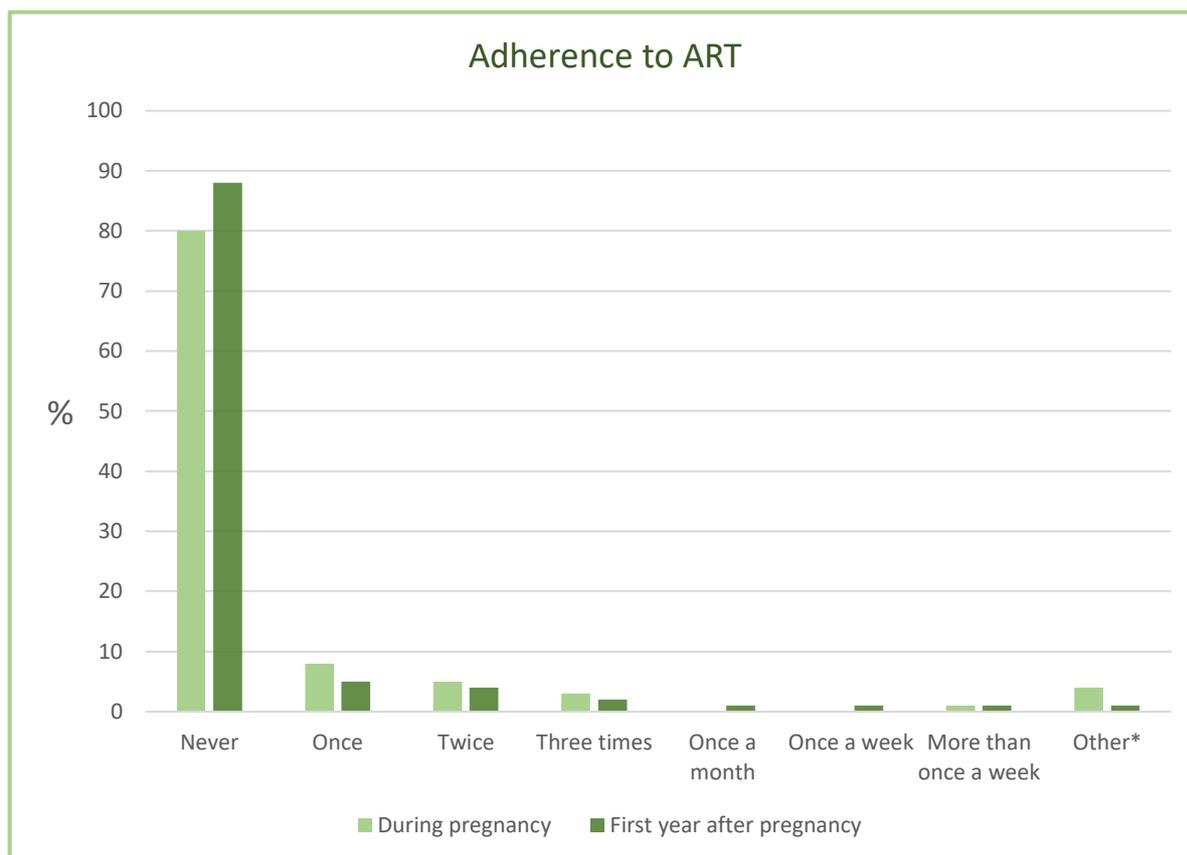


Figure 4. The mothers’ adherence to ART based on the questions “How often did you miss to take your ART during your pregnancy?” and “The first year after your baby was born, how often did you miss to take your ART?”. * = Four times, five times, bad adherence first month, one week.

The reasons for suboptimal adherence were forgetting to take the medicine (7 of 26), being away from home (5 of 26), and avoiding side effects (6 of 26). Other less frequent reasons were ART being out of stock (3 of 26), not wanting others to notice (2 of 26), and problems taking them at specific times (1 of 26). Eight mothers had other reasons for not taking their pills, where four of them were connected to the birth of their babies.

There was no significant difference in adherence between mothers who were diagnosed with HIV during the pregnancy compared to women who had been diagnosed prior to the

pregnancy ($p = 0.18$ regarding adherence during pregnancy and $p = 0.88$ regarding adherence after birth). Nor was there a significant difference in adherence between mothers who started ART immediately compared to mothers who waited before initiating treatment ($p = 0.45$ regarding adherence during pregnancy and $p = 0.74$ regarding adherence after birth).

7.4 Postnatal follow-up

A summary of the compliance to WHO guidelines regarding postnatal follow-up that was found at KHC is presented in Fig. 5. Infant prophylaxis had been given to 91% of the babies. Seven of 103 babies had not received treatment and two of the mothers did not know. Among infants that received prophylaxis, 87% had received it for six or twelve weeks, 9% had been treated for a shorter period (between five days and four weeks), and 4% of the mothers did not know how long the treatment had lasted. Thus, 80% of the total number of babies had been given infant prophylaxis for the recommended period of time. The majority of the babies (93%) had an additional CTX-prophylaxis.

The majority (83%) of the babies had been tested for HIV at six weeks of age, 15% had not been tested and 2% of mothers did not know.

Nearly all mothers (99%) had been breastfeeding their babies. Most of them had been breastfeeding exclusively for six months (47%) or were still exclusively breastfeeding (41%).

Slightly more than one third (36%) of the babies had stopped breastfeeding at least six weeks before the interview. Nearly half (43%) of them had been tested six weeks after cessation of breastfeeding. The majority (49%) had not been tested and 8% of mothers did not know.

Only 14% of the babies were 18 months or older. Almost two thirds (57%) of them had been tested at 18 months of age, 29% had not been tested, and 14% of the mothers did not know.

All babies were asymptomatic, and none of them had therefore been tested because of HIV-associated symptoms.

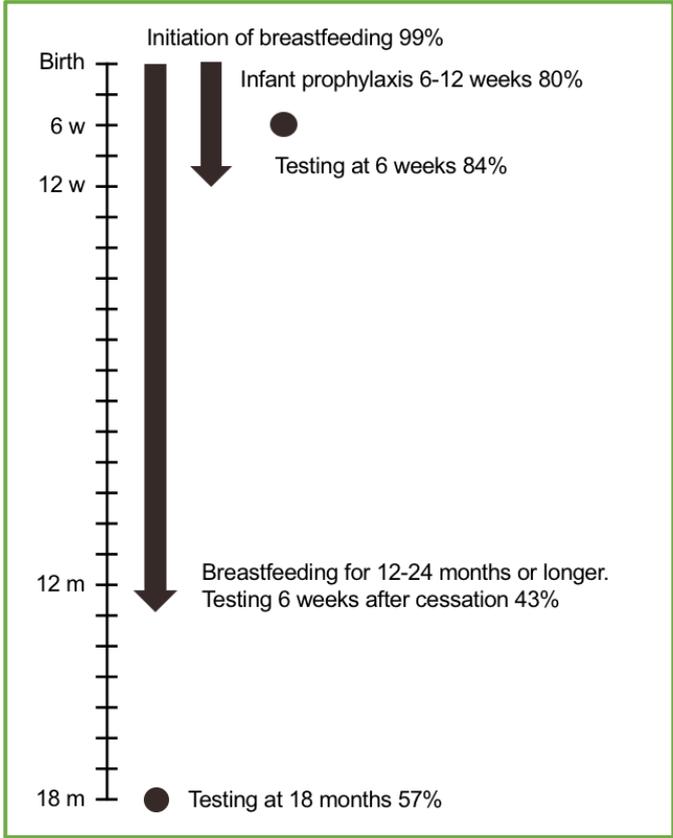


Figure 5. A summary of WHO guidelines on postnatal follow-up plotted in a timeline from birth to 18 months of age and to what extent they were being followed at KHC. All mothers but one initiated exclusive breastfeeding immediately. Eighty percent of the babies were treated with infant prophylaxis. At six weeks of age, 84% of the babies had been tested for HIV. The testing rates six weeks after cessation of breastfeeding were lower, only 43% were tested. At 18 months of age, 57% had been tested.

One child (1%) had been infected with HIV. He was tested positive at the first test at six weeks of age. The baby received ART immediately and at the time of the interview, he was eight months old and had never had any symptoms of HIV. His mother was diagnosed with HIV two years prior to his birth. She was on ART during the pregnancy but did not remember the name of the drugs. According to self-reported answers, she was fully adherent to ART during pregnancy and after birth. Her baby had received NVP for six weeks and CTX thereafter. She had been breastfeeding him exclusively for six months and was still breastfeeding.

7.5 Sociodemographic factors

Sociodemographic data is presented in Table 2. The mothers' ages were between 18 and 40 years (mean 27, median 28). The majority of the mothers (58%) belonged to the most common tribe in this area, Baganda. Most of them (41%) were Catholics. Being married was the most common form of civil status (74%). Almost all mothers were either working with unskilled labour or housekeeping. Half of the mothers had started but not finished secondary school, a fourth had not completed primary school and a fourth had completed it.

There was no significant correlation between sociodemographic factors and compliance with guidelines or adherence to ART.

Table 2. Sociodemographic factors among the mothers.

What is your ethnicity?	N (%)	What is your religion?	N (%)
Baganda	60 (58)	Protestant	22 (21)
Banyankole	12 (12)	Catholic	42 (41)
Basoga	8 (8)	Muslim	24 (23)
Other*	23 (22)	Born again	14 (14)
		Other**	1 (1)
What is your marital status?	N (%)	What kind of work do you do?	N (%)
Never been married	4 (4)	Farming	10 (9)
Married or cohabiting	76 (74)	Unskilled labour	46 (45)
Divorced or separated	22 (21)	Skilled labour	2 (2)
Widowed	1 (1)	Student	1 (1)
		Housekeeping	44 (43)
What was the last level of schooling that you completed?			N (%)
Primary school incomplete			26 (25)
Primary school complete (7 years)			25 (24)
Secondary school incomplete			48 (47)
Secondary school complete (5-6 years)			2 (2)
Post-secondary or more			1 (1)
Student			1 (1)

* = Alur, Anacholi, Bachiga, Bagishu, Bulundi, Iteso, Munkoyo, Munyarwanda, Munyoro,

Teso. ** = 7th day Adventist.

8. Discussion

8.1 Compliance to WHO guidelines

Among the 103 women living with HIV and their children included in the study, only one baby had become infected with HIV, resulting in a MTCT rate of 1%. However, 41% of the babies included in the study were still breastfeeding and had not yet reached the point where there was no more risk of acquiring HIV through MTCT. A transmission rate of 1% could therefore be an underestimation but indicates that the rate is low. The transmission rate was lower than national numbers, 2.9% in 2015, (11) and can be compared to high-income countries, such as Sweden, where the transmission rate was lower than 0.5% in 2017 (17).

Regarding compliance to WHO guidelines, 80% of the babies had received recommended infant prophylaxis. Seven babies had not been given infant prophylaxis, only CTX-prophylaxis. In HIV-positive infants and children who have been treated with CTX against opportunistic infections, greater survival has been shown (41). Due to the risk of acquiring HIV and not receiving immediate ART, the potential positive outcomes are considered to outweigh the risks with the treatment.

Some of the mothers stated that the reason for not receiving NVP was because it was out of stock at KHC. Lack of resources in the health care is a problem in Uganda, where only 1.4% of GDP is spent on health care by the government (14). If health care would have been more prioritized, there is a possibility that all babies could have been offered infant prophylaxis. In this study, economic issues with seeking health care were not studied. However, mothers complained about expensive transportation costs when they needed to travel to KHC more often because ART was out of stock. AAAQ (availability, accessibility, acceptability, quality) is used as a frame for the right to health with the goal that all people should receive essential

health care. Accessibility implies access to a health facility that one can afford to visit (42). Further research needs to be done to investigate if accessibility to health care is limited at KHC.

Early infant diagnosis, testing the baby before two months of age, is crucial to identify HIV-infected infants and quickly enroll them in care to minimize the very high mortality among untreated infants. The compliance to guidelines regarding testing was high at six weeks of age. Due to the risk of acquiring the infection during breastfeeding, it is of utmost importance to test the babies again when there is no more risk of acquiring HIV. Testing of babies after cessation of breastfeeding and at 18 months of age was insufficient at KHC and should be improved, so that infected babies can be identified. A final status serological test is important to rule out HIV. At KHC, rapid diagnostic tests that detect antibodies are used. An improvement could be made by changing to combination tests that detect both antigen and antibodies, to earlier detect HIV both in pregnant women and their babies.

Breastfeeding increases the risk of MTCT by 14%. However, as the situation is today, the benefits of breastfeeding outweigh the risk of acquiring HIV in Uganda. In low-resource settings, breastfeeding has been shown to decrease mortality in pneumonia, diarrhea, and undernutrition, which are all major causes of death in children under five (36). At KHC, mothers were recommended exclusive breastfeeding for six months with introduction of complementary foods thereafter. Nearly all mothers had been breastfeeding exclusively for six months or were still exclusively breastfeeding. The health staff followed the previous WHO recommendations from 2010, to advise mothers to stop breastfeeding at twelve months of age. However, WHO stated in 2016 that breastfeeding should continue for 12-24 months or longer, until a safe diet containing all necessary nutrients can be given (36), which is not yet

part of Ugandan Guidelines and has not been implemented at KHC. As time goes by, Uganda together with other low-income countries will hopefully get closer to the situation where high-income countries are, with low rates of child mortality. There is a possibility that in the future, breastfeeding will not be needed to protect the infants and children from severe infectious diseases, with decreased MTCT-rates as a result.

A study on PMTCT in Uganda showed that 96% of the babies had been given NVP prophylaxis, which is a higher coverage than at KHC. Regarding testing, 76% had been tested for HIV, nearly all of them during the first two months of life. The testing rates were lower than at KHC regarding early infant diagnosis. All of the mothers breastfed their babies, compared to all but one in this study. No baby was reported as HIV-positive, but not all had been tested and 24% of the mothers did not return for their children's results. A transmission rate of 0% could therefore be misleading. However, the results indicate that compliance to guidelines is correlated with a low risk of transmission (43). The design of this study differed from ours, in that they investigated if mothers were retaining in their PMTCT programmes by following women living with HIV over time. In our study, observations were done at a specific time point and mothers who did not seek health care at that time were therefore missed, which was a limitation of the study. Their study setting was in urban areas in the two largest cities in Uganda in medical facilities by The AIDS Support Organization, where better results could be expected than at KHC. Their conclusion was that the mothers retained in their PMTCT programmes to a high extent, whereas in this study, conclusions can be drawn only about the quality of the services given to people who are enrolled in care.

8.2 Adherence

Adherence to ART among the mothers was higher after delivery than during pregnancy, 85% and 79% respectively were fully adherent. These results were somewhat unexpected. Previous studies have shown that mothers tend to be less compliant after birth. A review found the adherence levels to be 53% postnatally compared to 76% during pregnancy, possibly due to the mothers' fear of transmission to the baby during pregnancy that decreases after birth (44). A qualitative study on adherence to ART in pregnant women in Uganda also mentioned decreased fear of infecting the baby together with being too busy taking care of the baby as reasons to poor adherence postnatally (45).

One explanation to why the results in our study differ from others could be that most mothers at KHC started ART the same day they were diagnosed without receiving enough information, which could lead to poor adherence in the initial stage. As time goes by and the mothers receive more information and counselling, they understand the importance of adherence and become more motivated. The health staff at KHC was most likely contributing to that. During the mothers' visits, they focused on adherence and emphasized that being compliant to ART postnatally, until cessation of breastfeeding, lowers the risk of transmission to the baby substantially. There was however no statistically significant difference in adherence between mothers diagnosed with HIV before pregnancy compared with those diagnosed during pregnancy. In the study mentioned above, immediate initiation of treatment is also discussed as a problem and they suggest waiting until the mother is prepared for it (45). The risks with waiting could be losing the mothers to follow up or exposing the babies to a risk of transmission.

8.3 Knowledge about HIV

The mothers' knowledge was high regarding vaginal sex as a transmission route and using condoms as protection. Their knowledge was poor in all other aspects. A large limitation to these results is that the questions were asked as open questions and later categorized. The mothers probably answered the first alternative that came in mind, vaginal sex as a transmission route and using condoms as protection. It is therefore most likely that the mothers' knowledge about HIV that was found is underestimated.

In UDHS (Uganda Demographic and Health Survey), a report focusing on knowledge about HIV and AIDS amongst others, the participants were prompted with specific questions, an approach that would have been more favourable in this study as well. The results from UDHS 2016 were that knowledge about protection by usage of condoms was 87% in women and 88% in men and limiting sexual intercourse to one uninfected partner 94% in women and 92% in men (46). UDHS 2011 had a section on MTCT, where 86% answered that HIV can be transmitted via breastfeeding and 78% that the risk can be reduced if the mother is taking drugs during pregnancy (47). The numbers in UDHS indicate higher knowledge than in this study, which could be explained by the difference in how the questionnaires were designed.

8.4 Methodological considerations

There were some limitations to the study. Firstly, all obtained information was self-reported. To minimize the recall bias, inclusion criteria were formed to exclude mothers with children older than three years of age. There is however a risk that the mothers could have thought that their care would benefit from answering what they thought was expected of them. This limitation is mainly applicable to the questions about adherence.

Also, using an interpreter when conducting interviews is a source of error. Interpreting is not equal to translating and I could not be certain that my sayings were correctly conveyed to the mothers and that the answers I received were correct. The interpreter was a nurse at KHC, which could have had an impact on the liability of the answers. She was however not their caregiver, but a volunteer working at the medical ward, which implies less bias. The risks of receiving dishonest answers were reduced by informing the participants that the study was confidential and relying on the trust between a patient and a healthcare worker. The benefits of using an interpreter were that the questions could be explained which lowered the risk of misunderstandings.

A strength with this study was that response rates were high. Only one mother declined to participate. The sample group that was included in the study is therefore likely to be a good representation of the population of mothers living with HIV that are receiving health care at KHC. However, when the mothers were interviewed they were asked to approach us one by one, which implies a risk for selection bias.

The patients that visited KHC were living in peri-urban and rural areas. The vast majority of people in Uganda live in rural areas, 84% in 2014 according to the World Bank (48). The prevalence of HIV in Kampala region does not differ much compared to other areas (49). KHC is a governmental health centre, which means that they are governmentally funded and are following guidelines from Uganda Ministry of Health. There is no obvious way to why other governmental facilities in peri-urban and rural areas of Uganda would differ from KHC and one could speculate that the numbers would be similar in other places. Generalising the results and conclusions of the study to a larger population in Uganda is therefore possible.

However, more studies including more mothers in different geographic locations would give a better understanding of the situation.

This study found that among mothers receiving health care at KHC there was a low rate of MTCT of HIV. However, no information was obtained about the mothers who did not seek health care. A study that evaluated PMTCT-programmes in Kenya stated that 43% of mothers diagnosed with HIV during the pregnancy were lost to follow-up (50). Further research needs to be done to understand why mothers are lost to follow-up and what can be done to prevent that from happening.

Finally, as this is a cross-sectional study, causality cannot be claimed. The conclusion that compliance to guidelines could lead to low MTCT-rates can be indicated but is not proved by this study.

9. Conclusions and implications

In conclusion, it was found that WHO guidelines are being followed to a large extent at KHC, which probably is an important explanation for the low rate of MTCT (1%) that was found. Even though the health centre has limited resources and the prevalence of HIV in Uganda is among the highest in the world, the transmission rate is nearly as low as in high-resource countries such as Sweden (0.5%). KHC has made great achievements and should be a good example for other medical facilities in settings with a high prevalence of HIV.

The mothers were more adherent to ART after birth than during pregnancy, 85% and 79% respectively, perhaps because they were diagnosed with HIV during the pregnancy. No significant difference was however found between the groups.

The mothers' poor knowledge about transmission of HIV and protection against transmission that was found was probably an underestimation caused by the design of the questionnaire.

This study found that mothers who were visiting KHC regularly received adequate health care. To further decrease and eliminate MTCT, more research needs to be done to understand the situation for mothers who do not receive health care, why they are being lost to follow-up and what can be done to prevent that from happening.

10. Populärvetenskaplig sammanfattning

Förebyggande av mor-barn överföring av HIV på Kasangati Health Centre, Uganda

Varje dag smittas 400 barn under 15 år av den obotliga infektionen HIV (humant immunbristvirus), främst i fattiga områden i världen. I över 90% av fallen sker överföringen från mor till barn under graviditet, vid födsel eller via amning. Om de smittade barnen inte får behandling kan det få förödande konsekvenser med stor sjuklighet och dödlighet som följd. I Uganda, ett av de länder som har drabbats hårdast av HIV-epidemin, har man fokuserat på att förebygga mor-barn överföring av HIV och år 2016 behandlades mer än 95% av gravida kvinnor med bromsmedicin, vilket minskar smittorisken kraftigt. Trots de stora framgångarna måste mammor och barn följas upp bättre efter förlossningen för att överföringen ska kunna elimineras. I Uganda testades endast en tredjedel av barnen för HIV innan två månaders ålder år 2015 och inte ens hälften av de HIV-infekterade barnen behandlades med bromsmedicin år 2016.

Syftet med denna studie är att undersöka uppföljningen av mammor med HIV och deras barn efter förlossningen på ett hälsocenter, KHC (Kasangati Health Centre), i utkanten av huvudstaden Kampala i Uganda. För att undersöka detta genomfördes tolkade intervjuer med hjälp av enkäter baserade på riktlinjer från WHO (World Health Organisation).

Totalt 103 kvinnor över 18 år vars yngsta barn var mellan sex veckor och 18 månader gammalt inkluderades via mödravården eller HIV-mottagningen. Av dessa hade enbart ett av barnen smittats med HIV. WHO:s riktlinjer följdes i stor utsträckning, 80% av barnen behandlades enligt rekommendationerna med bromsmedicin i sex till tolv veckor. Vid sex veckors ålder hade 84% av barnen testats för HIV. Dock hade endast 47% testats sex veckor efter avslutad amning. Vid 18 månaders ålder hade 57% testats. Inget av barnen testades på grund av symptom som talade för HIV, då alla saknade sjukdomstecken.

Studiens resultat tyder på att arbete i enlighet med riktlinjer spelar stor roll vid mor-barn överföring av HIV och att man genom att följa riktlinjer kan förhindra stor sjuklighet. På KHC är överföringen av HIV låg trots knappa resurser, detta genom stort fokus på denna kategori av patienter, men också genom en medvetenhet hos mammorna om möjligheterna att minimera risken att deras barn drabbas av deras egen sjukdom. De har trots kraftigt mycket högre förekomst av sjukdomen nästan lika låg smittöverföring som i Sverige, en stor bedrift!

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Appendix 1

Questionnaire

Prevention of mother-to-child transmission of HIV at Kasangati Health Centre, Uganda

Hello, my name is Emina Coric and I am a fifth-year medical student at Gothenburg University in Sweden. I am working on a research project about prevention of mother-to-child transmission of HIV.

The survey will take about 15 minutes. Your participation in the interview is voluntary. You can choose not to answer all the questions and decide to stop the interview at any time. All of the information will be kept confidential.

Interview information

1.1 *Interview ID number in the form of 001, 002, 003...*

1.2 *Date of interview DD/MM/YYYY*

1.3 *Clinic*

HIV

Firstly, I am going to ask you a few questions about your HIV diagnosis and your knowledge about HIV.

2.1 **When were you diagnosed with HIV?**

2.2 **Are you taking antiretroviral treatment (ART)?**

yes no

declined to answer

2.3 **When did you first start taking ART?**

Knowledge about HIV transmission

3.1 **What are some of the ways HIV can be transmitted?**

Mark all that apply.

vaginal sex

oral sex

blood transfusion with
HIV-infected blood

anal sex

sharing a needle or syringe when
injecting drugs

from mother to child during
pregnancy

- from mother to child during birth
- from mother to child during breastfeeding
- other, please specify:
- don't know

3.2 What are some ways that an HIV-positive person can reduce the risk of transmitting the virus to another person through sexual contact?

Mark all that apply.

- use condoms
- abstain from sex
- stay with one partner whose status one is sure of
- reduce the number of partners
- other, please specify:
- declined to answer
- don't know

Adherence to ART during pregnancy and postpartum

I am going to ask you some questions about your pregnancy with your youngest child and the care of the baby after giving birth. Please answer all the questions with your youngest child in mind.

4.1 How many children do you have?

4.2 How many times have you been pregnant?

4.3 When was your youngest child born?

4.4 Were you taking ART during your pregnancy?

- yes, please specify which:
- yes, don't remember which
- no
- started during pregnancy, please specify which month:
- declined to answer

4.5 How often did you miss to take your ART during your pregnancy?

- never
- once a month
- once a week
- more than once a week
- other, please specify:
- declined to answer
- don't know

4.6 Did you continue with the same treatment after your baby was born?

- yes
- no – I changed to:
- no – I stopped taking ART
- declined to answer
- don't know

4.7 The first year after your baby was born, how often did you miss to take your ART?

- | | |
|---|--|
| <input type="checkbox"/> never | <input type="checkbox"/> once a month |
| <input type="checkbox"/> once a week | <input type="checkbox"/> more than once a week |
| <input type="checkbox"/> other, please specify: | <input type="checkbox"/> declined to answer |
| <input type="checkbox"/> don't know | |

4.8 What circumstances led you to miss taking your ART?

- | | |
|---|---|
| <input type="checkbox"/> forgot | <input type="checkbox"/> was away from home |
| <input type="checkbox"/> pill burden | <input type="checkbox"/> pills were out of stock |
| <input type="checkbox"/> avoid side effects | <input type="checkbox"/> didn't want others to notice |
| <input type="checkbox"/> felt like the drug was toxic/harmful | <input type="checkbox"/> had problems taking them at specific times |
| <input type="checkbox"/> felt sick/ill | <input type="checkbox"/> other, please specify: |
| <input type="checkbox"/> declined to answer | <input type="checkbox"/> don't know |

Postnatal care: HIV testing and breastfeeding

5.1 Did your baby get infant prophylaxis to prevent HIV?

- | | |
|---|-------------------------------------|
| <input type="checkbox"/> yes | <input type="checkbox"/> no |
| <input type="checkbox"/> declined to answer | <input type="checkbox"/> don't know |

5.2 If yes, what kind of medication?

- | | |
|---|--|
| <input type="checkbox"/> nevirapine for six weeks | <input type="checkbox"/> nevirapine for twelve weeks |
| <input type="checkbox"/> other, please specify: | <input type="checkbox"/> don't know |

5.3 Was your baby tested for HIV at six weeks of age?

- | | |
|---|-------------------------------------|
| <input type="checkbox"/> yes | <input type="checkbox"/> no |
| <input type="checkbox"/> declined to answer | <input type="checkbox"/> don't know |

5.4 Did you breastfeed your baby?

- | | |
|---|---|
| <input type="checkbox"/> yes – exclusive breastfeeding for six months, then mixed feeding | <input type="checkbox"/> yes – exclusive breastfeeding for a longer period of time, please specify: |
| <input type="checkbox"/> yes – mixed (breastfeeding and replacement feeding) | <input type="checkbox"/> yes - still exclusive breastfeeding |
| <input type="checkbox"/> no – only replacement feeding | <input type="checkbox"/> other, please specify: |
| <input type="checkbox"/> declined to answer | <input type="checkbox"/> don't know |

5.5 If yes, was your baby tested for HIV six weeks after cessation?

- | | |
|---|--|
| <input type="checkbox"/> yes | <input type="checkbox"/> no |
| <input type="checkbox"/> declined to answer | <input type="checkbox"/> still breastfeeding |
| <input type="checkbox"/> don't know | |

- 5.6 Was your baby tested for HIV again at 18 months of age?**
- yes no
 declined to answer don't know
- 5.7 Was your baby tested for HIV due to symptoms suggesting HIV infection?**
- yes no
 hasn't had any symptoms declined to answer
 don't know
- 5.8 Has any of the tests been HIV positive?**
- yes – please specify which: no
 waiting for result declined to answer
 don't know
- 5.9 If any of the tests has been HIV positive, has your baby got ART?**
- yes no
 declined to answer don't know

Sociodemographic factors

Finally, I am going to ask you a couple of questions about you and your background.

- 6.1 How old are you?**
- 6.2 What is your ethnicity?**
- Baganda Banyankole
 Basoga other, please specify:
 declined to answer
- 6.3 What is your religion?**
- Protestant Catholic
 Muslim Pentecostal
 other, please specify: declined to answer
- 6.4 What was the last level of schooling that you completed?**
- no formal education primary incomplete
 primary complete (7 years) secondary incomplete
 secondary complete (5-6 years) post-secondary or more
 other, please specify: declined to answer
- 6.5 Are you...?**
- never married married or cohabiting
 divorced or separated widowed
 declined to answer

6.6

What kind of work do you do? By that I mean, what kind of activities keep you busy during an average day, whether you earn money from them or not.

Mark all that apply.

- | | |
|---|---|
| <input type="checkbox"/> farming | <input type="checkbox"/> fishing |
| <input type="checkbox"/> skilled labour | <input type="checkbox"/> unskilled labour |
| <input type="checkbox"/> student | <input type="checkbox"/> housekeeping |
| <input type="checkbox"/> none (no agricultural or housework?) | <input type="checkbox"/> other, please specify: |
| <input type="checkbox"/> declined to answer | |