

# Adherence and effectiveness of guidelines for prevention of mother to child transmission of HIV in Moshi, Tanzania

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# **Adherence and effectiveness of guidelines for prevention of mother to child transmission of HIV at Kilimanjaro Christian Medical Centre, Moshi, Tanzania**

**Master thesis in Medicine**

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**Gothenburg, Sweden 2014**

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## Abstract

Master Thesis, Programme in Medicine

Effectiveness and adherence to guidelines for prevention of mother to child transmission of HIV at KCMC, Moshi, Tanzania

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**Background** Mother-to-child transmission (MTCT) is the second most common mode of HIV transmission after heterosexual contact. The estimated rate of MTCT without any interventions is 25-40% but with the adequate prevention including HIV-testing, antiviral treatment and breastfeeding advices the MTCT could be less than 1%.

**Aim** To identify factors that influence MTCT of HIV.

**Method** An observation study was performed on the adherence among consecutive HIV-positive mothers to the current guidelines on prevention of MTCT of HIV.

**Results** In total 98 HIV-positive mothers with children born between 1998 and 2014 were included in the study, 26 of the mothers had a HIV-positive child, 43 had a HIV-negative child, 20 had children with unknown HIV-status and 9 were excluded due to insufficient data. The transmission rate of HIV during 2014 was 14%. The mothers with HIV-positive children had a lower CD4-count than the mothers with HIV-negative children ( $p=0.003$ ). The mothers who were diagnosed after delivery had a higher prevalence of infected children in comparison to those who were diagnosed before the pregnancy ( $p<0.004$ ). A tendency towards that the mothers with HIV-positive children received treatment to a lesser extent than those with HIV-negative children was seen ( $p=0.07$ ). The children who acquired the infection also received treatment to a lesser extent than the negative children ( $p<0.001$ ). Nevirapine prophylactic treatment to the child had the strongest impact on the MTCT and reduced the transmission rate with one fifth. It was also seen that exclusive breastfeeding for six months reduce the transmission rate with 43%.

**Discussion and conclusion:** This study showed that the rate of MTCT of HIV is strongly correlated on the extent of the adherence to the guidelines of prevention. The prevention programs of MTCT in the western world today are very effective and to halter the MTCT in developing countries the programs must be available and accepted by all pregnant women with a high compliance.

**Keywords:** HIV, prevention, pregnancy, resource limited settings

## Background

### Introduction

Human Immunodeficiency Virus (HIV) continues to be a major global public health issue and it is included as one of the ten leading causes to death worldwide defined by WHO [1]. In 2013 approximately 35.3 million people in the world lived with the disease and Sub-Saharan Africa has the highest rate where nearly one in every twenty adults live with the infection [2]. One of the targets in the UN Millennium Developing Goal six is to halt the spread of HIV/AIDS by 2015 [3] and great achievements have been done but still there is much to do to reach this goal.

HIV is a RNA retrovirus which infects CD4+ helper T –lymphocytes and the virus uses the host cell to multiply. When the virus burden increase as the disease develops the amount of CD4+ cells decreases through apoptosis. The decrease of CD4-cells enable opportunistic infections and/or tumours and the CD4+-count can be used to determine the degree of the immunosuppression [4].

HIV can appear in two different subtypes, subtypes 1 and 2. HIV-2 has remained largely restricted to West Africa and the subtype has both lower pathogenicity and transmission rate with near complete absence of mother-to-infant transmissions [5].

## **Treatment of HIV**

Unfortunately there is no available cure for HIV today. Antiretroviral therapy (ART) can be used to slow down the replication of the virus and there is also available treatment for some of the opportunistic infections and tumors. The first HIV-medicines was developed in the 80th but it was first in the 90th they become effective enough to treat the disease with reduced mobility and mortality [4]. Today the medicines are very effective and in high-income countries half of death are not related to AIDS among HIV-positive patients who receive ART [6].

The medicines can be divided into five groups based on their pharmacodynamics and they all work at different stages in the virus life's cycle. The groups are; entry/fusion inhibitors, nucleoside reverse transcriptase inhibitors, for example zidovundin (AZT) and lamivudin (3TC), none-nucleoside reverse transcriptase inhibitors, for example efavirenze (EFV) and nevirapin (NVP), integrase inhibitors and protease inhibitors.

The standard treatment today is a combination of tree different substances from two different groups [4]. This is often called highly active antiretroviral therapy (HAART) [36] or combined antiretroviral therapy (cART) and a successful combination can induce a huge reduction in the virus burden and enable the immune system to recover [4].

High adherence to the treatment is very important to control the disease and to minimize the risk of developing a therapy resistant infection. As long as a person is on medicine the virus cannot infect new cells. Even if one miss out on a small amount of doses it can cause a lower serum concentration of the medicine which can make it possible for the virus to start replicate.

An increase rate of replication will increase the risk of developing mutation which could makes the virus resistant to the treatment and it will also make the person more infective [4].

### **Classification of HIV**

Staging and classification systems are critical tools for both tracking and monitoring the epidemic and clinical management. Today there are two major classification systems; the U.S. Centers for Disease Control and Prevention (CDC) classification system and the World Health Organization (WHO) Clinical Staging and Disease Classification System. The WHO system was developed in 1990 and it divides the disease into four stages where stage four is the most advanced stage of the disease. The system is mainly based on clinical symptoms and parameters but a positive HIV-antibody test or other laboratory evidence of HIV infection is required to be able to use the system [7]. The CDC classification system contains three stages and it takes in account the CD4<sup>+</sup>-count and the 26 AIDS-defining conditions [9].

### **United Republic of Tanzania**

Tanzania is a Sub-Saharan country and border Indian Ocean in the east. The population is estimated to be around 45 million divided into thirty regions and Dodoma is the capital city. The country is a democratic republic but one party is dominant and elections is held every fifth year.

Tanzania is one of the poorest countries in the world. About half of the population is under 18 years of age and around three million children are orphans. The population is growing fast and the country lack resources to take care of the growing population. In the country, one third lives in poverty and one in five have not enough to eat every day [13].

Moshi Municipality is located in the north of Tanzania in the Kilimanjaro Region and the population is almost 200, 000. Moshi has one of the highest literacy rate for persons over 15 years of age in Tanzania [14] it is assumed to be the cleanest town in the country and the tourism is very important source of income like export of coffee and tea.

### **Prevalence of HIV in Tanzania**

The first case of HIV in Tanzania was reported in 1983 in the Kagera Region. Since then the prevalence has steady increased until the peak in 1997 when the prevalence was 8% [35]. The prevalence among adults today (age 15-45 in 2011-12) is 5.1 % [12] and the number is significantly higher in urban regions in comparison to rural areas [8]. Big differences are also seen within the country. Iringa Region had the highest prevalence where 15.7 % of the population was positive and Kilimanjaro Region, where the study been conducted, had one of the lowest prevalence where only 1.9% (age 15-49 in 2011-12) were positive [14].

### **Kilimanjaro Christian Medical Centre and Child Centred Family Care Clinic**

Kilimanjaro Christian Medical Centre, KCMC was established in 1971 and it serves daily about 1000 outpatients in Kilimanjaro Region. It is a university hospital which has 11 clinical departments, 450 beds and offers diagnostic and treatment options for various disease and conditions including HIV/AIDS.

The Child Centred Family Care Clinic, CCFCC was started in December 2007. The clinic provides care and treatment to both children infected with HIV/AIDS and to HIV-exposed children until vertical transmission could be excluded and their families under one roof, this



due to the fact that HIV/AIDS are considered to be a family disease. The vision of the clinic is to integrate both treatment and care, and the clinic works closely with the social service [15].

## Transmission of HIV

HIV infection can be acquired through sexual intercourse, exposure to infected blood and from mother to child during pregnancy, labour, delivery and breastfeeding. Heterosexual unprotected intercourse is the main route of spreading the infection both worldwide and in Tanzania and more than 90% acquired the infection this way [8]. The transmission probability per sex act depends both on the type of intercourse (See Table 1) as well as on the virus burden in the infected person [19].

Table 1. *Risk of transmission of HIV due to type exposure and stage of HIV diseases.*

Activity	Risk-per-exposure
Vaginal sex, male-to-female, studies in low-income countries	0.30% (1:333)
Vaginal sex, female-to-male, studies in low-income countries	0.38% (1:263)
Vaginal sex, source partner has late-stage disease	0.55% (1:180)
Receptive anal sex amongst gay men	0.82% (1:123)

During the first weeks of infections the virus burden increases rapidly and the person is highly infective. After a couple of weeks the immune system starts responding to the infection and the virus burden decreases and stabilizes on a level call "set point" and the person becomes less infective. The virus burden will later increase as the disease develops and the person will than become more infective again (See Figure 1) [4].

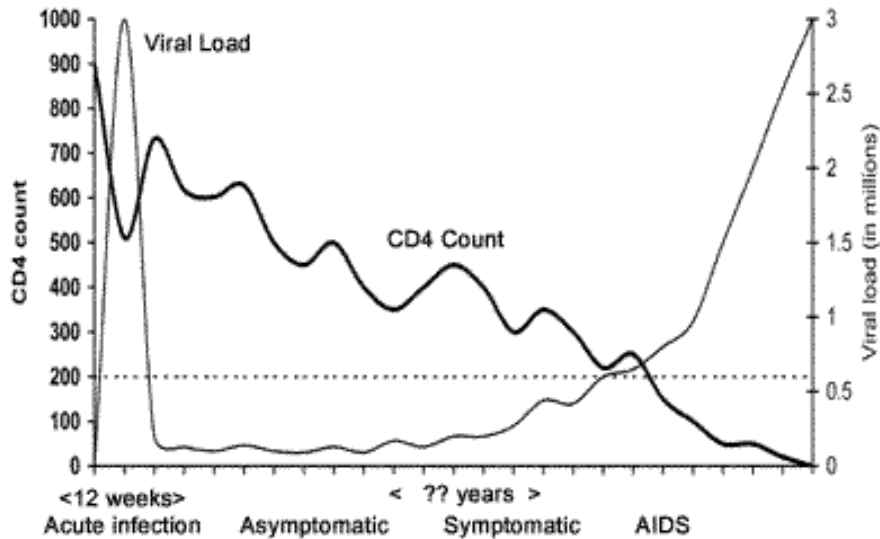


Figure 1. *Viral load and CD4-count in relation to stages of the disease* [21]

The infection can also be spread by other body fluids such as genital secretions, cerebrospinal fluid and amniotic fluid. Transmission resulting from exposure to saliva, urine or sweat is not very likely, if at all possible [8]. The second most common mode of transmission is Mother-to-child transmission (MTCT) or vertical transmission which contributes to over 90% of new infections in infants and young children [12] and around 20% of the new infection in the whole society [33]. Since there is no cure for HIV, primary prevention is the most effective means to control the spread and minimise its impact on individuals, families and communities.

### **Mother to child transmission of HIV**

A decline is seen in the number of children acquiring HIV infections through MTCT [3] but still there is more to be done. With the adequate prophylaxis including HIV-testing, antiviral treatment and breastfeeding advices the MTCT could be less than one percent [34] in comparison to 20-45% which is the estimated rate of transmission without any prevention (See Figure 2) [14].

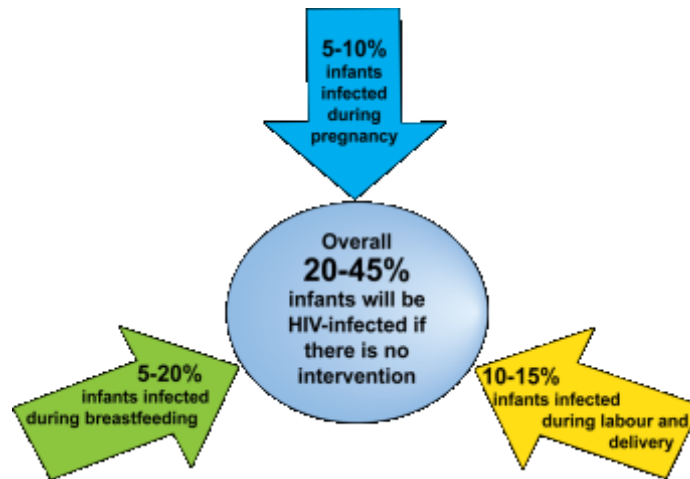


Figure 2. Estimated rate of transmission of HIV without any prevention.

There are many risk factors that increase the transmission rate during pregnancy, labour, delivery and breastfeeding. For example, different kinds of infections and high maternal viral load and a low CD4 count (See Table 2, Figure 2) [35].

Table 2. Risk factors for mother to child transmission of HIV.

During Pregnancy	During Labour and Delivery	When Breastfeeding
High maternal viral load and low CD4 count (new infection or advanced AIDS)	High maternal viral load and low CD4 count (new infection or advanced AIDS)	High maternal viral load and low CD4 count (new infection or advanced AIDS)
Viral, bacterial or parasitic placental infections (e.g., malaria)	Chorioamnionitis (from untreated STIs or other infections)	Oral disease in the infant (e.g., thrush or mouth sores)
STIs	Rupture of membranes for more than 4 hours before delivery	Breast abscesses, nipple fissures, and mastitis Long Duration of breastfeeding
		Mixed feeding (i.e., breastfeeding combined with other foods or fluids) before 6 months of age

To reduce and minimise the transmission rate Prevention of MTCT-programs (PMTCT-programs) have been developed. The goal of the PMTCT-programme in Tanzania is virtual elimination of MTCT of HIV by 2015. Virtual elimination refers to 90% reduction in estimated number of new infants infection and an HIV infants transmission rate of <5%,

which is associated with at least 90% of all the HIV-exposed infants being alive and uninfected with the virus at the age of 2 years [35].

In Sweden the care of HIV-positive women is very advanced and the guidelines are highly implemented. The MTCT rate is lower than 1% [6] and during the past 10 years there is only 3 reported cases on children required the infection via the mother. These three mothers were all assumed to be well treated and at the time following the current national guidelines with high compliance.

## **National Guidelines for Comprehensive Care of Prevention of Mother-to-Child Transmission of HIV services in Tanzania**

The Ministry of Health and Social Welfare (MoHSW) in Tanzania has been implementing PMTCT services in the country since 2000. A scale-up and roll-out was done in 2003 to cover all the fourteen regions in the country. In 2004 national guidelines was developed and the current guidelines are based on national HIV/AIDS policies and strategies and also on WHO recommendations on PMTCT and infant feeding from 2010. Since 2010, in 2013, WHO updated theirs guidelines but those changes are not yet implanted in the current guidelines in Tanzania. The guidelines today includes; HIV-testing, comprehensive ANC, ART to the mother and prophylactic treatment to the child, safe delivery practises, counselling on safe infant feeding, postpartum care for mother and infant following-up tests (See Figure 3).

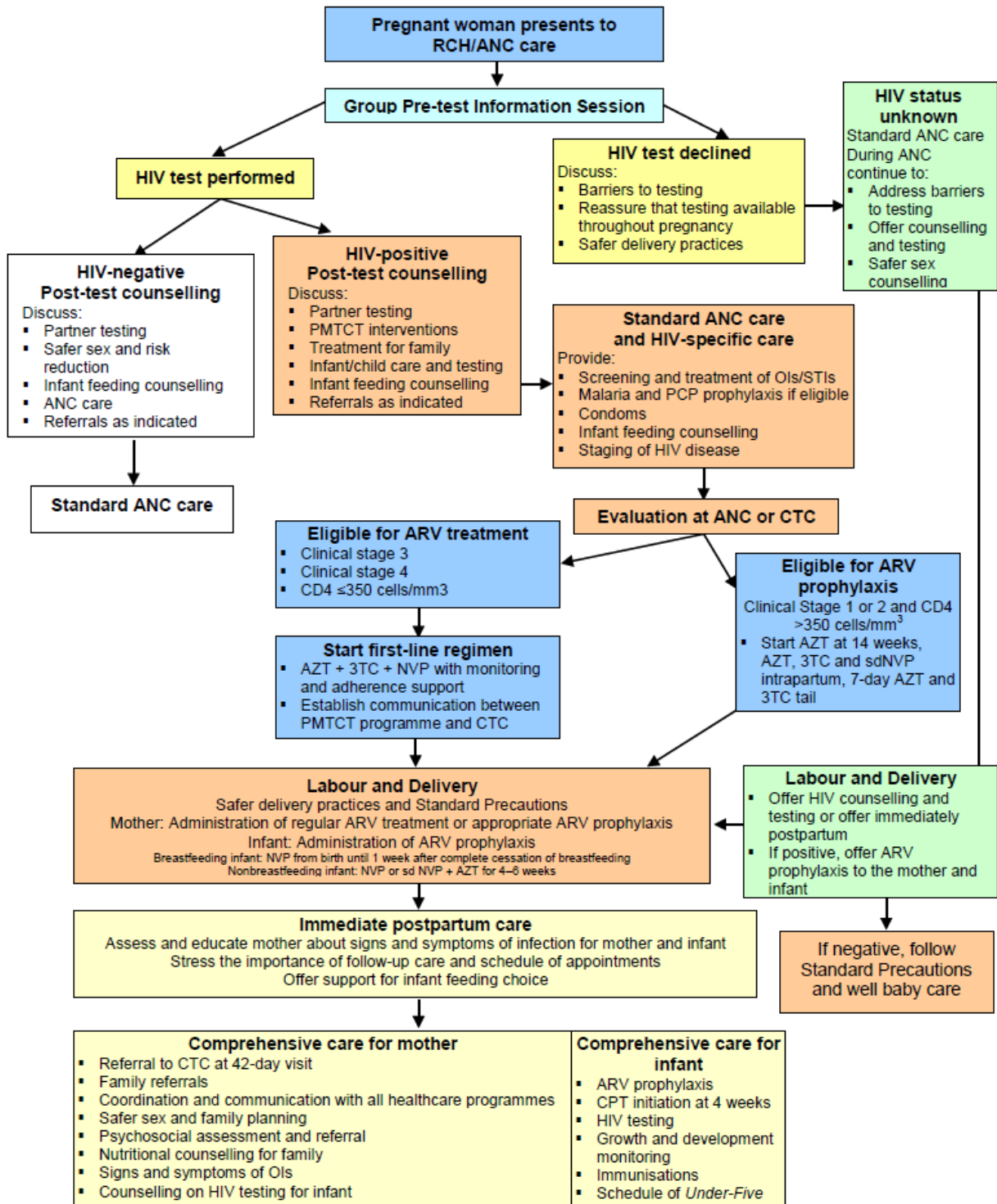


Figure 3. Handling of pregnant women at ANC or RCH.

## **HIV-testing**

All women should receive HIV testing with both pre and post-testing counselling at the first antenatal visit. A negative test should always be retested during the third trimester and partner should also be encouraged to be tested. The diagnosis of a HIV infection in adults is established by detecting HIV antibodies using simple rapid tests according to the national HIV rapid testing algorithm. The result of the test should always be given to the patient within the same day of testing combined with post-testing counselling regardless of the result.

Women in labour with unknown HIV status should receive a rapid HIV test as it is important that ARV prophylaxis can be administered as soon as possible.

All HIV-exposed infants should have an initial PCR HIV-test at the age of 4 to 6 weeks. Infants who has a negative first HIV-test will need two repeat HIV-test, one additional PCR-test at six weeks after complete cessation of breastfeeding and one antibody test (either rapid tests or ELISA or a combination of both) at 18 months of age. At 18 month of life the antibodies from the mother are assumed to be disappeared and the antibody tests can be reliably used to diagnose the infection in the same manner as in adults.

## **Antenatal care**

Pregnant women living with HIV should attend ANC clinic every month to ensure high adherence to treatment. The visits should also include a full delineation of the women health situation with physical examinations, laboratory testing, HIV-staging, counselling on PMTCT, healthy delivering and infant feeding advices, ART or ARV and vaccinations.

The women should be offered cotrimoxazole 960mg daily through the pregnancy to reduce the risk of getting any opportunistic infection or other infections during the pregnancy.

The women should also receive nutritional counselling throughout the antenatal period and nutritional supplements if needed. Before discharge from the labour ward the mother should be administered vitamin A.

### **Antiretroviral treatment to mother and child**

Antiretroviral treatment (ART) is used both to treat the maternal infection and to reduce the risk of transmission from the mother to the infant. Treatment to the mother reduces related morbidities which improves the survival chances of the child and it also decreases the viral load in the mother which reduces the infant's exposure to HIV with results in a reduced in the risk of acquire the infection.

The eligibility for ART can be determined by clinical staging or by the CD4-count. If the pregnant woman is eligible for treatment it should start as soon as possible and continue throughout pregnancy, childbirth, breastfeeding and thereafter. If a woman already is on ART the regular dosing schedule should continue throughout labour and delivery, as well as during the postpartum period. In some cases there is a need to change the medications. For example, efavirenz should not be used during the first trimester because it may causes birth defects and nevirapine regimes should then be used instead.

Eligibility criteria for ART to a pregnant women living with HIV;

- CD4 cell counts of  $\leq 350$  cells/mm<sup>3</sup>, irrespective of WHO clinical staging or
- WHO clinical stage 3 or 4, irrespective of the CD4 cell count.

The first line of ART regimes is AZT + 3TC + EFV or AZT + 3TC + NVP. The treatment should always be coupled with once daily administration of NVP to infants from birth or as soon as possible and thereafter until 6 weeks of age, regardless of infant feeding choice.

Women not eligible for ART should receive or antiretroviral prophylaxis (ARV) with AZT 300 mg twice a day from as early as 14 weeks of gestation and no postpartum treatment is assumed to be needed in those cases. This treatment should as well always be coupled with daily administration of NVP to infants from birth or as soon as possible and thereafter until 6 weeks of age, regardless of infant feeding choice. (See Figure 5).

### **Implementation of safer obstetric practices**

Safe obstetrics includes; using standard precautions, minimise vaginal examinations, avoiding prolonged labour and unnecessary trauma during delivery, misnaming the risk of postpartum haemorrhage and using safe transfusion practices.

Caesarean section performed before the onset of labour or membrane rupture has been associated with reduced MTCT. However, in Tanzania, the capacity to perform caesarean sections is low and it is not recommended for the purpose of reducing MTCT. The only indicated for caesarean section should be obstetric reasons.

Healthcare workers should strongly encourage all women to give birth at facilities where skilled health care workers can address potential complications and provide care that will reduce the risk of MTCT.



## Infant feeding

Mothers wishing to reduce the risk of transmitting HIV to their infants should either choose to exclusive replacement feed their infants or breastfeed exclusively for the first 6 months of life. However, exclusive replacement feeding is only recommended when it is assumed to be AFASS (acceptable, feasible, affordable, sustainable and safe) (See Table 3). The current general advice is therefore to breastfeed exclusively for the first six months of life and then introduce complementary foods while continuing to breastfeed to 12 months of life. The child should be receiving ARV prophylaxis for 6 weeks regardless of feeding option. If the child is confirmed as HIV-positive the mother are recommend to breastfeed the child until 24 months of age [35].

Table 3. *Definitions of different infant feeding options.*

<p><b>Exclusive breastfeeding</b> = Feeding infant <i>ONLY</i> breastmilk and no other liquids or solids, with the exception of drops or syrups consisting of vitamins, mineral supplements or medicines prescribed by a healthcare worker.</p> <p><b>Replacement feeding</b> = Feeding infant something <i>OTHER THAN</i> breastmilk. During the first 6 months of life, the only replacement feed that meets an infant's nutritional requirements is commercial infant formula.</p> <p><b>Mixed feeding</b> = Feeding both breastmilk and other liquids (such as water, tea, formula, animal milk) or foods (such as porridge or rice).</p>
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## New guidelines for prevention of MTCT from WHO

The greatest differences between the recommendations from WHO 2010 and 2013 are regarding the treatment to the mother. In the guidelines from 2013 it is recommend that countries follow option B+ and in countries where this is not feasible, option B should be applied. Option A is now only cited as a last resort (See table 4). As writing there is an ongoing work in implanting the new guidelines from WHO in the daily work at CCFCC.

Table 4. *Treatment options for pregnant HIV-positive women.*

**Option B<sup>+</sup>:** A triple-drug antiretroviral regimen which should be taken throughout pregnancy, delivery, breastfeeding and continuing for life, regardless of CD4 count or clinical stage.

**Option B:** A triple-drug antiretroviral regimen should be taken throughout pregnancy and delivery. If the mother is breastfeeding, she should also continue to take the triple-drug antiretroviral regimen up to 1 week after breastfeeding has finished.

**Option A:** One antiretroviral regime with AZT daily during pregnancy and one week post-partum.

Efavirenz should today be one of the three drugs in the first line regime regardless of trimester. This due to the fact that it can be used in all women, regardless of CD4 count unlike nevirapine, which cannot be used in women with high CD4 counts because of the risk of severe side effects. Although concerns remain about the safety of efavirenz in early pregnancy but the benefits are likely to outweigh the risks [16, 17].

Another difference from the old recommendations is the view on co-trimoxazole as prophylactic treatment against various infections. The recommendations today are stricter and co-trimoxazole should only be used when the HIV disease is severe (WHO clinical stage 3 and 4, or CD4  $\leq$ 350 cells/mm<sup>3</sup>) and in settings with high prevalence of malaria and/or severe bacterial infections regardless of WHO clinical stage or CD4 cell count [18].

## **Aim**

- To investigate the adherence among HIV-positive mothers to the current guidelines for PMTCT of HIV in Tanzania.
- To investigate the effectiveness of the current guidelines for PMTCT of HIV in Tanzania.
- To investigate the knowledge about HIV/AIDS among HIV-positive mothers in Tanzania.

## **Methods**

The study took place at CCFCC, KCMC during 11 weeks in October to December, 2014.

### **Study design**

The study was conducted as an empirical observation study of the adherence among HIV-positive mothers to the current guidelines of PMTCT of HIV in Tanzania. The study had a positivistic view with quantitative gathering of data. The data was collected via questionnaires. The questionnaire was prepared on forehand in Sweden and presupposed from the current guidelines in Tanzania. The questions were later translated from English into Swahili by two fifth year medical students at KCMC. To prevent misunderstandings the questions were initially tested on a pilot group of ten mothers and then slightly improved. The questionnaire was handed out to the mothers during the concealing meeting that was held by three different nurses at the clinic every morning. The mothers mainly filled in the

questionnaire by themselves but I or one of the three nurses were available at all time if any of the mothers needed clarifications or help with reading or writing.

## **Study population**

The sample consisted of 98 consecutive HIV-positive mothers at CCFCC.

## **Variables in the study**

Data was abstracted in the questionnaires regarding;

- General information about the mother including age, number of children, marital status, living condition, location of residence, level of education and profession.
- Specific information about the mother including number of HIV-test, time of diagnosis, CD4-count, duration and type of treatment.
- Adherence and compliance to treatment and recommendation regarding PMTCT of HIV among the mothers.
- Knowledge about HIV/AIDS among the mothers regarding routes of transmission, prevention of transmission, infant feeding and prevalence as well as where the mother had get the most useful information and from where they wish to get more.
- Regarding the child; age, HIV-status and management.

## **Statistical methods**

Data analyses were done using Microsoft Office Excel 2007. Comparisons between groups were performed using Fisher's exact test if  $n > 5$  otherwise chi square tests were used. T-test were used to compare mean values. P values  $< 0.05$  were considered statistically significant.

## **Ethical considerations**

The clients were informed in Swahili that participation in the study was voluntary. They were also informed that whether or not they chose to participate, the treatment at the clinic would not be affected. Neither the mothers nor the children in the study are able to identify. The clients had to sign a consent form (See appendix 1) before the start of the participation in the study and the consent form will not be a part of further analysis.

Ethical approval was obtained from Kilimanjaro Christian Medical College and University Ethical Committee.

## Results

### Epidemiology

In total 98 mothers was included in the study, 26 mothers had a HIV-positive child, 43 had a HIV-negative child, 20 mothers had a child with unknown HIV-status and 9 were excluded due to insufficient data. The median age of the mothers was 35 years. The mothers to the HIV-positive children had a median age of 38 years and the mothers of the HIV-negative children had a lower median age, 33 years ( $p=0.002$ ). In total 40% of the mothers were married but the prevalence of widows was higher among the mothers with HIV-positive children in comparison to the mothers with HIV-negative children ( $p=0.03$ ). Only one third of the mothers had told their partner about their HIV-status and there was one mother how have not told anyone in her surrounding about her HIV-status. Almost half of the mothers lived in rural area and the other half in urban areas. A trend was seen that it was more common among the mothers with HIV-positive children to live in rural areas but this was not statistically significant. Almost all, 87/89 (98%) of the mothers had been to school. The majority had went to primary or secondary school and only 9/89 (10%) had a university degree (See Table 5).

Table 5. *Epidemiology of the mothers.*

Characteristics	Mothers with HIV-positive children	Mothers with HIV-negative children	P-value	Total
Median age, years	38 (n=25)	33 (n=44)	0.002	35
Number of children, average	2	2		2
Married	8/26 (31%)	22/43 (55%)	-	36/89 (40%)
Widows	8/26 (31%)	2/43 (5%)	0.03	4/89 (4%)
Location of residence, urban area	8/26 (31%)	22/43 (51%)	0.42	41/87 (47%)
Location of residence, rural area	15/26 (58%)	20/43 (47%)	0.42	41/87 (47%)
Went to primary or secondary school	25/26 (96%)	36/44 (82%)	-	87/89 (98%)
Went to high school or university	3/26 (12%)	3/44 (7%)	-	9/89 (10%)

The median age of the children was 4 years, range 0-16 years, and the mothers had in average two children. The children were in average born in week 37 and 34% of the children were delivered via caesarean section. Almost all of the children, 88% were born at a hospital or health care centre and no statistically significant difference was seen neither in location of birth or way of delivery between the children how acquired the infection or not (See Table 6).

Table 6. *Epidemiology of the children.*

Characteristics	
Median age, years	4 (0-16)
Median delivery week	37
Caesarean section	27/80 (34%)
Delivery at hospital/health care centre	67/76 (88%)

### Knowledge about HIV/AIDS among the mothers

The median age for when the mothers first had heard about the disease HIV/AIDS was 23 years and no statistically significant differences was seen between the mothers with HIV-positive and HIV-negative children (See Figure 4).

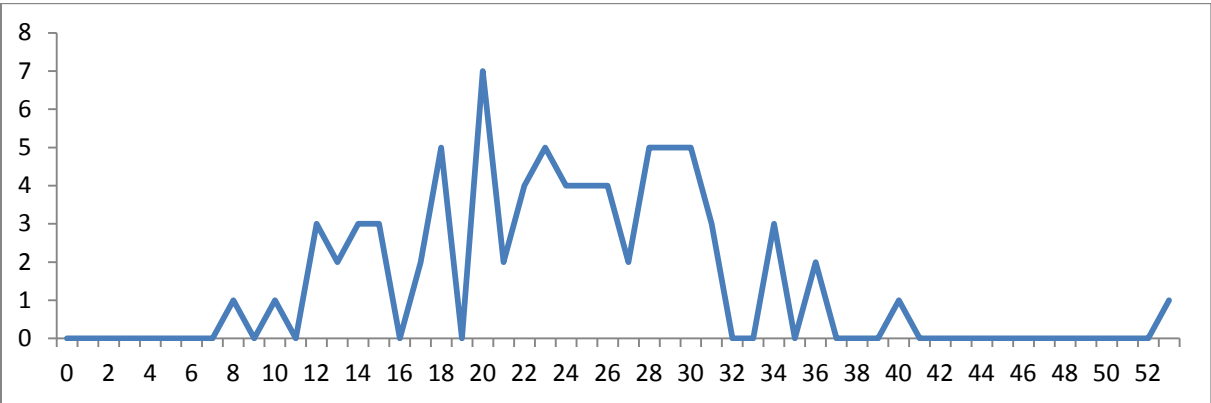


Figure 4. *Age of the mothers for when they first heard about HIV/AIDS.*

More than half of the mothers, 40/75 (53%) believed that the prevalence in the area where they lived were higher than 50% and only seven mothers, 7/75 (9%) estimated correctly the prevalence to be between 1-10% (See Table 7).

Table 7. *Knowledge among the mothers.*

	Percents, %, of the mothers
Estimate the prevalence to >50%	53 (40/75)
Estimate the prevalence to 1-10%	9 (7/75)
<b>Awareness of transmission modes of HIV</b>	
Sexual intercourse	98 (86/88)
Heterosexual intercourse as the main route of transmission	87 (62/71)
Mother to child transmission	55 (48/88)
Breastfeeding	38 (33/88)
<b>Awareness of prevention modes for MTCT of HIV</b>	
Treatment to mother	41 (35/85)
Treatment to child	33 (28/75)
Believed there is a cure of HIV/AIDS	29 (24/83)
Available treatment for HIV/AIDS	65 (56/86)

Almost everyone of the mothers, 86/88 (98%) knew that HIV could be spread via sexual intercourse without condom and 62/71 (87%) knew that unprotected heterosexual intercourse was the main mode of transmission in the area they were living in.

The level of knowledge regarding PMTCT was very low. Only 48/88 (55%) knew that HIV can be spread from mother to child during pregnancy and delivery and only 33/88 (38%) mothers knew that it can be spread via breastfeeding. Less than half of the mothers, 35/85 (41%) knew that medicine to the mother could prevent the transmission and 28/75 (33%) mothers knew that medicine to the child could prevent transmission.

One in every third mother, 24/83 (29%) believed that there is a cure for HIV and only 56/86 (65%) mothers knew that there is available treatment with reduction and prevention of related symptoms.

Half of the mothers, 39/83 (47%) reported that they got the most useful information about the disease from the health care system and 62/81 (77%) reported that they would like to get more information about the disease from the health care system.



No statistically significant differences were seen between the mother with HIV-positive and the mothers with HIV-negative children in the level of knowledge regarding general knowledge and routes and prevention of transmission of HIV/AIDS.

### **Effectiveness and adherence to the guidelines for PMTCH of HIV**

The mothers with a HIV-positive children had a lower CD4-count in comparison to those with HIV-negative children (398 versus 628, n=22, p=0.003).

The transmission rate of HIV from the mother to the child during 2014 at CCFCC was 4/22 (14%) and 1/11 (9%) during 2013 (See Figure 5).

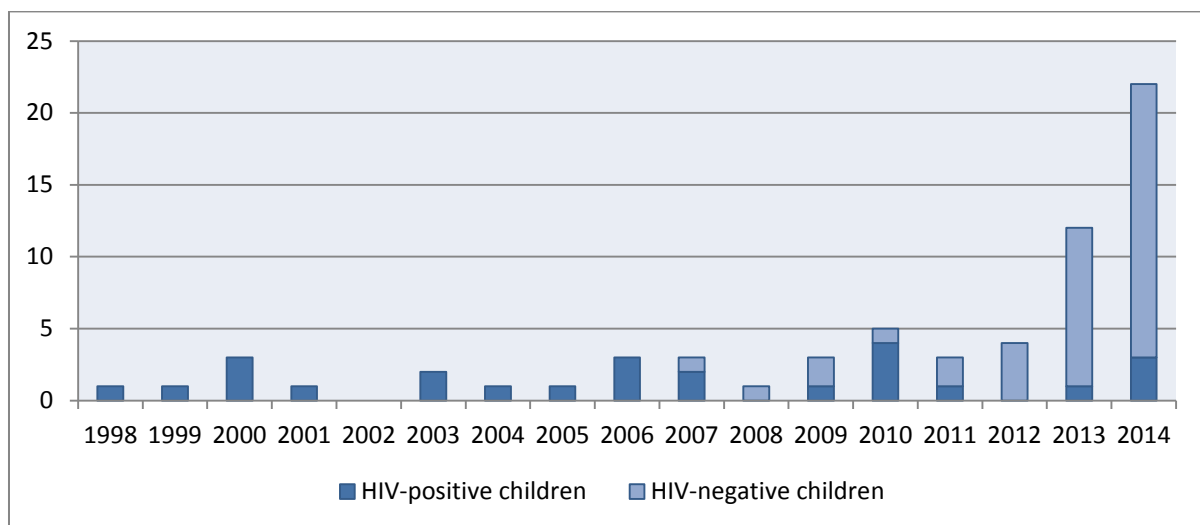


Figure 5. *The number of HIV-positive and HIV-negative children at CCFCC 1998-2014.*

In those four cases where transmission occurred during 2013-14, one child was premature, one mother was diagnosed during the pregnancy, had a low CD4-count and low adherence to the ART, one was diagnosed after the delivery and one reported low adherence to the ART and prematurity as risk factors for transmission (See Table 8).

Table 8. *Reported risk factors for vertical transmission among the mothers-child pair were the transmission occurred 2013-14.*

	Time of diagnos	CD4-count	Treatment	Delivery	Prophylactic treatment to the child	Exclusive breastfeeding, 6 months
<b>Mother 1</b>	Before pregnancy		Stated before pregnancy High adherence	Week 32 Caesarean section	NVP, 6 weeks	Yes
<b>Mother 2</b>	Week 28	163	Started in w 28 Low adherence	Week 38	NVP, 6 weeks	Yes
<b>Mother 3</b>	After delivery	353				
<b>Mother 4</b>	Before pregnancy		Started before pregnancy Low adherence	Week 36	NVP	Yes

### HIV-testing of mother and child, and times of diagnosis of the mothers

The mothers had in average 2.7 HIV-tests in their life and no differences were seen between the mothers with HIV-positive and HIV-negative children. It could though be seen that the mothers with HIV-positive children was diagnosed later than the mothers with HIV-negative children. Among the mothers with HIV-positive children 10/25 (40%) were diagnosed after delivery but only 2/43 (5%) of the mothers HIV-negative children ( $p=0.004$ ). It could also be seen that diagnosis before pregnancy reduced the transmission rate of HIV to 65% (RR=0.65, 95% CI 0.25-0.84) (See Table 9).

All children in the study had been offered at least one HIV-test.

Table 9. *Risk factors for mother to child transmission of HIV.*

	Mothers to HIV-positive children	Mothers to HIV-negative children	P-value	Risk ratio
CD4-count, mean value	398 (n=9)	628 (n=13)	0.003	-
Location of residence, urban area	8/26 (31%)	22/42 (51%)	0.42	-
Location of residence, rural area	15/26 (58%)	20/42 (47%)	0.42	-
Diagnosis before pregnancy	11/25 (44%)	32/43 (74%)	0.01	0.65 (95% CI 0.25-0.84)
Diagnosis after delivery	10/25 (40%)	2/43 (5%)	0.004	3.11 (95% CI 1.89-5.14)
Recived general advices regarding HIV/AIDS	18/24 (75%)	41/41 (100%)	0.001	0.31 (95% CI 0.2 -0.45)
Treatment to mother	21/25 (81%)	38/43 (89%)	0.07	0.8 (95% CI 0.36-1.80)
Delivery via caesarean section	6/24 (25%)	18/42 (43%)	0.17	-
Exclusive breastfeeding for six months	17/21 (81%)	42/44 (95%)	0.08	0.43 (95% CI 0.22-0.87)
Prophylactic treatment to the child	4/19 (20%)	19/20 (58%)	<0.001	0.19 (95% CI 0.075-0.46)

### **Antenatal care and safer obstetric practices**

As shown in the table 8, delivery via caesarean section tend to be more common among the mothers with HIV-negative children in comparison to the mothers with HIV-positive children, 18/42 (43%) versus 6/24 (25%) but this difference turned out to be not statistically significant ( $p=0.17$ ).

### **Antiretroviral and prophylactic treatment to mother and child**

A tendency was seen that ART were more common among the mothers with HIV-negative children than among the mothers with HIV-positive children, 38/43 (89%) versus 21/25 (81%), ( $p=0.07$ ) (See table 8).

Prophylactic treatment with nevirapine daily to the child for the first six weeks of life were more common among the HIV-negative children than among the HIV-positive children.

Among the HIV-positive children, 4/19 (21%) had received prophylactic treatment and 19/20 (95%) among the HIV-negative children ( $p<0.0001$ ). Prophylactic treatment to the child had the strongest impact on the transmission rate of HIV. The treatment reduce the risk of transmission from the mother to the child to 19% (RR=0.19, 95% CI 0.01-0.46).

### **Infant feeding**

A tendency towards that exclusive breastfeeding for six months were more common among the mother with HIV-negative children than among the mothers with HIV-positive children was seen. Among the mothers with HIV-negative children, 42/44 (95%) were breastfeeding exclusive but only 17/21 (81%) among the mothers with HIV-positive children ( $p=0.08$ ).

Exclusive breastfeeding reduced the rate of transmission of HIV from the mother to the child with 43% (RR=0.43, 95% CI 0.22-0.87).

## Discussion

The results in this study shows that there is a strong relationship between the adherence to the guidelines for prevention of MTCT of HIV and the transmission rate of HIV from the mother to the child during pregnancy, labour, delivery and breast feeding.

The transmission rate of HIV from the mother to the child during 2014 at CCFCC in this study was 14% and 9% in 2013. In an earlier survey in Kilimanjaro Region where 561 HIV-exposed children were followed in regard to the PMTCT components provided the transmission rate of HIV between January 2009 and August 2012 was 9.6% [22]. This findings can be compared with other related studies on HIV transmission rate in other PMTCT programmes. A study in Angola showed a MTCT rate of 1.5% (1/66) [24] and another study in Guangdong province in China showed a rate of 6.7% [23]. Both studies were executed before the 2013 WHO recommendations. In a study from Côte d'Ivoire the transmission rate was as high as 16.1% even though the mothers received treatment according to the PMTCT programme [25]. In Sweden the transmission rate is as low as 0.6% when looking at all exposed children in the country between 1999-2003 [26]. As seen, the transmission rate differs in those studies between 0.6-16% even though all the mother-children pairs were including in preventions programmes. This difference can be due to the fact that it is hard to accomplish high adherence in resource limited settings to all the steps within the programmes which is necessary to reach a low transmission rate. It can also be due to the fact that the programmes are less advance in resource limited settings, for example replacement infant feeding is not the general recommendation in Tanzania which it is in Sweden and also the treatment recommendation varies between countries.

First, diagnosis of the mother. It was seen in this study that it was more common with diagnosis of the mother after the delivery among the mothers with HIV-positive children than among the mothers with HIV-negative children. Diagnosis before pregnancy reduced the transmission rate to 65% and it is of course an essential step in the prevention of the transmission of the infection. It has earlier been seen that that most vertically infected children are transmitted through lost preventive opportunities [37].

Secondly, treatment to the mother were slightly less common among the mothers with HIV-positive children than among the mothers with HIV-negative children. In total 87% of the mothers did receive treatment and treatment seems to reduce the transmission rate but this could not be shown as statistically significant, probably due to the limited sample size in the study. In the study in Kilimanjaro Region [22], 93% of the mothers received treatment and a strong association was then seen between treatment and reductions of infection in the children. This findings have also earlier been seen in many studies, for example in Angola where no ART to the mother were associated with a 5-fold higher infant risk of HIV transmission or death (3).

Another problem discovered in this study is that the latest recommendation for PMTCT treatment to the mother is not implemented in the current national guidelines. The guidelines in Tanzania was developed in 2012 and based on the WHO's recommendations from 2010. In June 2013 WHO updated their recommendations for antiretroviral treatment to HIV-positive mothers and those recommendations are unfortunately not yet implanted in the national guidelines in Tanzania. However, there is an ongoing work in implanting the new guidelines in the daily work in clinics around the country including at CCFCC. Studies are pointing on that the new guidelines both has a positively impact on the health and being cost-saving. A

cohort study from Zambia on 600, 000 pregnant women from March 2014 suggest that the shift from 2010 Option A to the 2013 guidelines would result in a 33% reduction of the risk of HIV transmission among exposed infants. The study also suggest that it would be cost-saving in the long term as it spares future treatment costs by preventing infections in infants and partners [27].

Thirdly, treatment to the child turned out to have the greatest impact on the MTCT of HIV in this study. It was seen that 60% of the children received prophylactic treatment and it was more common among the HIV-negative children than among those how acquired the infection ( $p < 0.001$ ). Prophylactic nevirapine daily to the child for six week reduce the transmission rate to one fifth in the study. According to a Cochrane review from 2014 based on seven RCT antiretroviral treatment to is efficacious in reducing HIV transmission [28].

Fourthly, exclusive breast feeding for six months also had a strong impact on the transmission rate of HIV in the study. A tendency towards that exclusive breast feeding were more common among the HIV-negative children than among the HIV-positive children was seen and in total 91% of the children were exclusive breast fed. In the survey from Kilimanjaro Region [22], it was seen that 89% of the children were exclusive breastfed and that it tended to reduce the MTCT but without being statistically significant. The effectiveness of exclusive breast feeding has though been seen in many other studies before. In a study from Nigeria, more than 80% of exposed babies screened for HIV were breastfed, but the risk of MTCT was 50% higher for children who were given mixed feeds than for those who were exclusively breastfed or given replacement feeding [29] and similar results are seen in studies from Ethiopia [30].

It was also shown in the study that the general knowledge about HIV among the mothers was surprisingly low. It was seen that the median age among the mother for when they first heard about HIV was 23 years. In Tanzania, the mean age for sexual debut was 16.5 and 17.0 years of age for respectively males and females and no contraceptive use was reported by 29.7% of the males and 40.3% of females [31]. Heterosexual contact is the main route of transmission the infection in the country and primary preventions is an essential step in the process to stop the spread of HIV.

The level of knowledge regarding PMTCT of HIV was also seen to be very low. For example only 55% of the mothers knew that HIV could be spread from mother to child during pregnancy, labour and delivery and only 38% knew that it could be spread while breast feeding. Only 41% knew that treatment to the mother could prevent MTCT and only 33% knew that treatment to the child also could prevent transmission. This is lower in comparison to what have been seen in other studies. In a study in Dar es Salaam published in 2013 on 383 pregnant women in a peri-urban area a higher level of knowledge was seen. For example, a majority of the respondents, 96.3% were aware of the possibility of an infected pregnant woman transmitting infection to her unborn child [32].

One third of the mothers also believed that there is a cure for HIV/AIDS.

No differences were seen between the mothers with HIV-positive and the mothers with HIV-negative children regarding the knowledge about HIV/AIDS. If the general knowledge was high among the mothers this would have been a desirable result but since it is rather the opposite this is quite stunning. This due to the fact that the mothers with HIV-positive children meets an doctor at CCFCC every second month until the child is around 16 years old

and regularly attending counselling meetings held by the nurses at the clinic which does not exist at the regular HIV-clinic for adults at KCMC. This actions was expected to result in a higher awareness among the mothers at the clinic.

## **Limitations and methodological considerations**

An obvious bias in this study is of course recall bias. Over time it is easy to forget and remember thing incorrectly. Both the mothers and the children where transmission occurred were older which may enhance the recall bias in that group. The guidelines and recommendations has also been modified over time with also could enhance the bias among the mothers with HIV-positive children.

Another potential bias is the risk of the participants not being completely honest in their replies. This regarding two aspects, both due to that clients does not want to admitted that they missed dozes or not followed the recommendation as they were supposed to or due to that they are afraid of the consequences if the child had acquired the disease. To avoid this the clients was on forehand informed that the study was confidential and that it would not affect their visit at the clinic in any manner.

The questionnaires was made in English on forehand and translate into Swahili on arrival by two fifth year medical students at KCMC witch of course could lead to misinterpretations. However, I or one of the three nurses involved in the study was always available for clarifications of any kind.



Another weakness with the study is that it only contains reported information. The study would have been more reliable and broader if it was combined with information from the mother files regarding for example duration and type of treatment, CD4-count and year of diagnosis. Due to different circumstances this was impossible. In the future it would be interesting to compare data from the files with reported data from the clients.

The sample size was too small to get statistical significance when small differences were seen. Another problem with the sample is that it is only possible to count the transmission rate two years back due to the fact that the HIV-negative children after that become discharged from the clinic.

## **Conclusion**

This study showed that the rate of MTCT of HIV is strongly correlated on the extent of the adherence to the guidelines on prevention of MTCT. The transmission rate was shown to be quite high at CCFCC which means that there is room for improvement. It was seen that prophylactic treatment to the child and safe infant feeding significantly reduced the transmission rate. It was also seen that in those cases where transmission occurred the mothers were diagnosed later, had a lower CD4-count and had received treatment to a lesser extent in comparison to those who had HIV-negative children.

To reach the goal of virtual elimination of MTCT of HIV by 2015 established by MoHSW all women in Tanzania must be included in the prevention programmes with a high adherence as well as that the new guidelines from WHO must fully be implemented.

## Populärvetenskaplig sammanfattning

### Utvärdering av mor-barn-överföringen av HIV i Tanzania

I studien på 98 HIV-positiva mödrar i norra Tanzania under hösten 2014 sågs det att man kunde minska överföringsfrekvensen av HIV från mor till barn med en femtedel via att enbart ge smittförebyggande behandling till det nyfödda barnet under dess första sex levnadsveckor. Det sågs även att man kraftigt kunde reducera överföringsfrekvensen via att enbart ge amningsråd till de nyblivna mödrarna.

HIV är ett av vår tids största hälsoproblem. Ungefär 35 miljoner människor i världen lever med sjukdomen och förekomsten är som högst i Afrika söder om Sahara där nästan var tjugonde person är drabbad. I dagsläget finns ingen botande behandling för sjukdomen vilket gör arbetet med att minska spridningen till ett essentiellt steg i begränsandet av sjukdomen. HIV sprids via samlag, från mor till barn under graviditet, förlossning och amning samt via blod. Överföringsfrekvensen från mor till barn i västvärlden är mindre än en procent om man följer de rådande rekommendationerna från WHO som bland annat innehåller tillvägagångssätt för diagnostisering av modern, behandlingsråd till både mor och barn samt riktlinjer för förlossning och amning. Utan några interventioner ligger överföringsfrekvensen mellan 25-45%.

Överföringsfrekvensen under 2014 var enligt studien 14% och det sågs att de rådande rekommendationerna i många fall inte följdes. Till exempel, 17% diagnostiserades först efter födseln, 14% av mödrarna fick ingen behandling och 36% uppgav att de inte tagit behandlingen enligt förskrivningen, 40% av barnen fick ingen smittförebyggande behandling och 10% ammade på ett icke önskvärt sätt. Sammantaget bidrog detta till den höga överföringsfrekvensen sedd i studien.

För att i framtiden minska sjukdomsördan till följd av HIV måste nu handläggandet av de HIV-positiva mödrarna drastiskt förbättras i Tanzania. Samtliga kvinnor måste få ta del av de rådande rekommendationerna med en hög följsamhet. Tidigare studier har visat att det är både hälsofrämjande och ekonomisk gynnsamt för ett land att implementera de senaste rekommendationerna från WHO på ett effektivt sätt.

## Acknowledgments

I would like to sincerely thank all persons that took part in this study and to the mothers who volunteered to participate in this study!

A special thanks also to Prof. Rune Andersson, University of Gothenburg and Dr. Rune Philemon at KCMC for their supervision, assistance and guidance throughout the project.

I am also grateful for the help of head nurse Zawadiel Hillu and the whole staff at CCFCC for assistance, translating and collecting data for the project.

Last, but not least I would like to thank my dear friend and study partner Stina Fredriksson for good collaboration and company.

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## Appendix I

### UTAMBULISHO

Habari. Jina langu ni..... mtafiti /muuguzi / muuguzi ninayefanya kazi KCMC/KCMU-College. Tunafanya utafiti tukishirikiana pamoja KCMU-COLLEGE /KCMC na chuo cha Gothenburg. Utafiti huu unaangalia uzingatiaji wa miongozo mipya ya kumkinga mototo dhidi ya maambukizi ya vvu.

Katika utafiti huu tungependa kukuhoji kuhusu huduma na ushauri uliopata kuhusu kumkinga mwanao dhidi ya maambukizi kulingana na miongozo mipya ya wizara ya afya na shirika la afya duniani. Lengo ni kupambanua mapungufu na mafanikio katika miongozo hii ilituweze kutoa mapendekezo ya kuiboresha na hivyo kufanikisha zaidi lengo kuu ambalo ni kukinga watoto wote dhidi ya maambukizi kwanjia ambazo nisahihi, rahisi na za kueleweka na kukubalika.

Taarifa utakazotupa katika mahojiano haya zitabaki kuwa siri kati yako na watafiti na zitatumika kwa lengo la kujifunza na kuboresha huduma. Wewe binafsi wala mwanao hamta tajwa katika kumbukumbu za utafiti huu na taarifa unazotupa hazita athiri huduma mnayo stahili kwa namna yoyote ile mbaya.

Kushiriki ni hiari na unaweza kutoka kwenye kuhusika na utafiti muda wowote, bila ya kubadili haki yako ya kupata huduma kwenye kliniki hii. Tungependa sana ushiriki na uwe huru kwenye kushiriki maana taarifa zenye usahihi zinazokusanywa kwa watu kama wewe ndio zimewezesha utaalumu wa kutoa huduma na jinsi tunavyoendelea kupata taarifa ndivyo huduma zinavyoweza kuboreshwa zaidi, kwako binafsi nahata kwa wengine ambao watahitaji huduma baada yako.

### TAMKO

Nimeeleweshwa kikamilifu kuhusu mtoto wangu kushiriki katika utafiti huu pamoja na athari na mazuri yake. Ninakubali kwa hiari kushiriki kikamilifu katika utafiti huu kwa faida ya afya ya watoto kama nilivyoelekezwa.

.....  
Sahihi ya mwongoza mahojiano

.....  
Sahihi ya mzazi/mlezi

.....  
Tarehe

.....  
Tarehe