Adherence to antiretroviral therapy among women living with HIV with previous participation in prevention of mother-to-child transmission programmes in Moshi, Tanzania

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Degree Project in Medicine

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1. ACRONYMS AND ABBREVIATIONS

AIDS	Acquired immune deficiency syndrome
ANC	Antenatal clinic
ART	Antiretroviral therapy
ARVs	Antiretroviral drugs
CCR5 antagonists	Chemokine receptor antagonists
CD4	Cluster of differentiation 4
CTC	Care and treatment clinic
FIs	Fusion inhibitors
HIV	Human immunodeficiency virus
INSTIs	Integrase inhibitors
KCMC	Kilimanjaro Christian Medical Centre
MTCT	Mother-to-child transmission
NNRTIs	Non-nucleoside reverse transcriptase inhibitors
NRTIs	Nucleoside reverse transcriptase inhibitors
PIs	Protease inhibitors
PMTCT	Prevention of mother-to-child transmission
WHO	World Health Organization

2. ABSTRACT

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Background
To optimize adherence to antiretroviral therapy (ART) in prevention of mother-to-child transmission (PMTCT) programmes, it is important to know ART adherence patterns among women. Increased knowledge of this can increase compliance to ART and further on decrease transmission of HIV from mother to child.

Aim
Investigate the effects of previous participation in PMTCT programmes on ART adherence among women living with HIV attending the PMTCT programme.

Methods
This cohort study was conducted at health centres in Moshi, Tanzania, March–April 2018. A semi-structured questionnaire was administered to women attending Care and Treatment Clinics and antenatal clinics. In addition, information from medical charts was collected. Adherence was defined as number of missed doses during the last week. Good adherence was defined as an intake of 95% or more.

Results
Twenty-one participants were enrolled. Nineteen women (90%) were adherent to their medication during the last week. Eight women (38%) had previously participated in a PMTCT programme and among those, two women had ended prematurely. There was no significant difference in ART adherence among mothers participating in the PMTCT programme for the first time compared to those who had participated before ($p = 0.51$).

Conclusion
Adherence rate among the women attending the PMTCT programme in Moshi is high. No correlation between previous participation in PMTCT programme and ART adherence was found.

Key words PMTCT, HIV, Medication adherence, Antiretroviral therapy

3. BACKGROUND

3.1 EPIDEMIOLOGY

In 2016, 36.7 million people in the world were living with HIV (human immunodeficiency virus) and 19.5 million of those were on antiretroviral therapy (ART) (1). HIV/AIDS (acquired immune deficiency syndrome) is globally the major reason of mortality among women of reproductive age (2). Although methods of prevention are known, 1.8 million people were newly infected during 2016 (1). Sub-Saharan Africa still remains the most HIV-affected region in the world and accounts for two-thirds of people living with HIV worldwide (3).

Tanzania is a country in eastern Sub-Saharan Africa with a population of 55.6 million (4). The first cases of HIV appeared in Tanzania in 1983 and since then the HIV epidemic has affected the entire society (5). In 2016, Tanzania had 1.4 million adults and children living with HIV and in the past ten years the prevalence merely has decreased from 6.6% to 4.7% among adults (15–49 years old), despite increased knowledge and roll-out of treatment (6).

3.2 HIV TRANSMISSION FROM MOTHER TO INFANT

Transmission of HIV can occur during sex, via blood products, through intravenous drug abuse, and from mother to infant (7). So called vertical transmission (mother to infant) can occur in-utero, intrapartum, or postnatally through breastfeeding with a mutual definition called mother-to-child transmission (MTCT) (8).

The risk of transmitting HIV from mother to infant is approximately 15–25% during pregnancy and delivery if no prophylactic interventions are initiated, with an additional 10–15% risk if the mother breastfeeds the baby (9). Interventions during pregnancy, delivery, and breastfeeding can reduce this risk to below 0.5% (10). Mainly, these interventions involve ART for the mother and prophylactic antiretroviral drugs to the child but also interventions of suitable feeding practices

(8). For instance, breastfeeding is fundamental in some regions in the world, since mothers can feed their infant with breast milk regardless of sanitation status and access to safe water (11).

High plasma viral load in the mother is the most important risk factor for transmission of HIV from mother to child during pregnancy, intrapartum, and postnatally (7). Other risk factors for MTCT during pregnancy are prematurity (before gestation week 34), sexually transmitted infections (STIs), and low $CD4^+$ levels (12) (13). Extended period from membrane rupture to delivery (14), chorioamnionitis (15), and vaginal delivery if the mother's viral load is high are some intrapartum risk factors (16). After delivery, mixed feeding (defined as giving both breastmilk and other fluids and/or food to an infant) to infants under the age of six months increases the risk of transmission (17). Mastitis in the mother and oral thrush in the infant have also been found to be risk factors postnatally (18, 19).

3.3 Antiretroviral therapy and adherence

ART is a combination of different antiretroviral drugs (ARVs), combined with the intention to decrease HIV RNA levels and prevent progression of the HIV disease (20). Six classes of antiretroviral drugs with different mechanism are registered. Generally, a combination of three ARVs is used to treat HIV. The six classes of ARVs are nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), integrase inhibitors (INSTIs), fusion inhibitors (FIs), and chemokine receptor antagonists (CCR5 antagonists). The exact combination for a specific patient depends on side-effects and resistance patterns for example (7).

To prevent MTCT of HIV it is important that pregnant women receive ART which can suppress the virus to undetectable levels (7). In 2016, the coverage of ART in pregnant women in Tanzania was 84% (6).

For breastfeeding or pregnant women, recommended first-line therapy is two NRTIs and one NNRTI (Tenofovir + Lamivudine/Emtricitabine + Efavirenz). Two measurements within three months with viral loads above 1000 copies/ mL after six months with new ART should be defined as viral failure. Recommended second-line therapy consists of two NRTIs + one ritonavir-boosted PI (21).

Adherence to ART can be explained as the voluntary ability to take the HIV medications in the exact manner written in the drug prescription which includes correct dosage and frequency. A well-recognized definition of good adherence is an intake of 95% or more of the doses. This definition is based on a study from 2000 when patients receiving PIs (with adherence over 95%) suppressed their viral loads to <400 copies/mL (22). In contrast, a meta-analysis from 2016, showed that adherence slightly lower than 95% also lead to viral suppression and the 95% definition should not prevent patients from receiving ART according to the authors (23).

Since the strongest risk factor for MTCT of HIV is the mothers viral load, adherence to treatment is of utmost importance (24). Unfortunately, optimal ART adherence has been shown to be a problem during pregnancy and postnatally, with approximately 25% of pregnant women having suboptimal adherence. Reasons for non-adherence are both economic and physical stress, depression, alcohol and drugs, and difficulties with medications (25). Factors associated with good adherence during pregnancy have been shown to be disclosure of HIV status and having treatment support (26). Inadequate knowledge about ART and prevention of mother-to-child transmission (PMTCT) are factors having negative impact on adherence among women living with HIV (27). Stigma on a community level has also been shown to be associated with suboptimal adherence (28).

3.4 Recommendations from WHO

Since 2015, WHO recommends lifelong ART to all pregnant and breastfeeding women regardless of clinical stage of disease or $CD4^+$ T-lymphocyte levels. This approach is called Option B+ even though there are no other options since 2015 (21). This has been implemented in Tanzania since 2013 (29).

During pregnancy, WHO recommendations include extensive HIV testing, pregnancy care to avoid hypertension and pre-eclampsia, and testing for other STIs (21). Delivery with supervision of competent caregivers is also recommended and the child should be washed from blood after delivery. WHO does not recommend elective caesarean sections in societies with limited resources to mothers living with HIV unless other obstetric indications occur (21).

The newborn should be given prophylaxis with one or two ARVs for 4-12 weeks depending on if the risk of transmission is considered high and if the mother breastfeeds the baby or uses commercial breastmilk substitutes (21, 30).

3.5 PMTCT programme in Moshi

The HIV testing rate is high among pregnant women in the Kilimanjaro region. In 2017, nearly 99% of pregnant women received HIV counselling, were tested for HIV, and received the result (31). Since 2004, Kilimanjaro Christian Medical Centre (KCMC) is offering free ART (32). All mothers living with HIV are recommended ART. CD4-levels and viral load measurements are available, but resistance-testing is very limited at KCMC due to the high cost (33). In 2015-2016, 91% of women living in the Kilimanjaro region gave birth in a health facility (34).

All pregnant women are offered a HIV-test at their first antenatal care visit. If a woman is diagnosed with HIV, she is included in the PMTCT programme and should thereafter attend the clinic once every month during pregnancy. The PMTCT programme is a part of the antenatal care

in Moshi. Blood samples are collected for analysis of HIV viral load, liver function tests, tuberculosis screening, and screening for STIs. In addition, regular delivery preparations will be done (35).

After delivery, the mother will continue to attend the PMTCT programme. Breastfeeding recommendations for all mothers in Moshi are exclusive breastfeeding for six months and after that breastfeeding for one year in combination with solid food and/ or commercial breastmilk substitutes. If the child is HIV-exposed (has an HIV-positive mother) and not infected one year after delivery the mother should stop breastfeeding. The child will be tested for HIV six weeks after delivery with PCR (HIV RNA), six weeks after cessation of breastfeeding with PCR (HIV RNA), and a confirmation test at the age of 18 months should be done with an antibody test (35).

3.6 MEDICAL RELEVANCE

To increase adherence to ART among pregnant and breastfeeding women in Tanzania it is central to analyse adherence patterns. Participation in a PMTCT programme has been offered to all pregnant women with HIV in Moshi Tanzania since 2004, but the outcome of this has never been studied. Therefore, the aim of my master thesis is to evaluate if there is a difference in ART adherence between women with previous participation in PMTCT programmes compared to women participating in the PMTCT programme for the first time. This knowledge will hopefully result in targeted efforts to increase the adherence and further on decrease the transmission of HIV to children.

4. AIMS

The primary aim was to investigate the effect of previous participation in PMTCT programmes on ART adherence among women living with HIV attending the PMTCT programme in Moshi.

Secondary aims were to analyse if previous participation in PMTCT programmes had an effect on the HIV status of the child/children and to investigate if socioeconomic status, education level, age, and knowledge of ART and PMTCT programmes affect level of adherence to ART.

5. MATERIAL AND METHODS

5.1 STUDY DESIGN:

This cross-sectional cohort study took place in Moshi, in northern Tanzania at the Care and Treatment Clinics (CTC) and antenatal clinics (ANC) at KCMC and Pasua Health Centre. KCMC is a large referral hospital and Pasua Health Centre is a public clinic with focus on people in disadvantaged socioeconomic classes.

Participants were enrolled in the waiting room at the clinics from the 7th of March until 18th of April, a total of 7 weeks. The women received oral information about the study, had the opportunity to ask questions, and thereafter gave their consent to participate in the study.

5.2 PARTICIPANTS:

- Inclusion criteria: Women living with HIV that were pregnant or had an infant younger than two months, attending CTC for follow-up in their PMTCT programme and women coming for their first delivery at antenatal care.
- Exclusion criteria: Mothers with an infant older than two months.

The number of patients differed from 0 to 6 per week. There was no non-completion due to denial of participation.

5.3 DATA COLLECTION:

To collect data, a semi-structured questionnaire was designed. When I arrived to Moshi I was told that my ethical application was denied so I could not participate in the distribution of the questionnaires. My tutor in Tanzania, Dr Philemon was conducting a study during the period of my stay in Moshi, analysing factors influencing adherence to breastfeeding amongst HIV-positive women which received ethical clearance from KCMUCo. He was going to collect data on ART also, even though it was not the primary objective so we incorporated my questionnaire in the one from this larger study. Due to this, my study had to have the same inclusion criteria's as the study conducted by my tutor. Since my ethical approval was denied, the start of the field study was delayed for three weeks leading to a small sample size and in addition, the number of enrolled patients each week was less than expected.

The questionnaire was available in Swahili and English and it was administered to participants by the research nurse Magdalena Otaro or Dr Philemon. They read the questions out loud and wrote down the answers. The clients' numbers were converted to a study id and this list was safely stored in a password protected computer.

The questionnaire contained questions regarding social and economic status, HIV status, previous and current participation in PMTCT programme, current ART (including adherence), side effects of ART, knowledge of ART and PMTCT recommendations, and infant feeding methods. Information was also gathered from medical charts about previous participation in PMTCT programme, ART prophylaxis, the woman's immune status, and HIV status of the children.

5.4 Definitions:

Adherence was defined as number of missed doses during the last week and good adherence as an intake of 95% or more of the doses.

5.5 Data analysis and statistical methods:

Data was analysed with descriptive statistics in SPSS. Frequency tables were used to describe patients' characteristics. To calculate mean and median values, the Mean-tool in SPSS was used. Chi-Square test with Fisher's Exact Test (Exact Sig, 2-sided) was used for univariate data to evaluate correlations between variables. P-values < 0.05 were considered statically significant.

6. Ethics

Participation in the study was completely voluntary. All women were given oral information about the study and thereafter gave their consent. There were no differences in the care and treatment of participants and non-participants. The primary study, which my study was incorporated into, received ethical approval from KCMU collage research ethics committee as well as permission from the Moshi Municipal Council, and the administration of the respective institutions.

7. Results

7.1 Characteristics of the participants

Twenty-one women were included in the study. Participant characteristics are shown in table 1. Eleven women from KCMC and ten from Pasua Health Centre were included. Median age of the participants was 30 and most of the women were employed or self-employed (in total 13/21).

One third of the women were married and 11/21 of the women had only finished primary school* and did not have any higher education. Christianity was the most common religion (16/21).

Table 1. Characteristics of the 21 participants.

Median Age		30 (Range 18-40)
Study site	PMTCT KCMC	11 (52)
	Pasua	10 (48)
Marital status	Married	7 (33)
	Single	5 (24)
	Co-habiting	3 (14)
	Separated	3 (14)
	Widow	2 (10)
	Divorced	1 (5)
Occupation	Self-employed	7 (33)
	Employed	6 (29)
	Housewife	3 (14)
	Unemployed	3 (14)
	Student	1 (5)
	Other	1 (5)
Education level	Never been to school	1 (5)
	Primary school (finished)	11 (52)
	Secondary school for 4 years	5 (24)
	Secondary school for 6 years	1 (5)
	Vocational college	1 (5)
	University	2 (9)
Current residence	Village	12 (57)
	Urban	9 (43)
Religion	Protestant	9 (43)
	Catholic	7 (33)
	Muslim	4 (19)
	Other	1 (5)

Data given as numbers (%).

* Seven years of primary school in Tanzania (age 7-13) (36).

7.2 HIV, ANTIRETROVIRAL THERAPY, AND SIDE-EFFECTS

The women had been diagnosed with HIV in median 46 months ago and the majority (13/21) had been tested at a health facility, primarily as a part of a PMTCT programme. The median number of living children per women was two. Two mothers had an HIV infected child and 2/44 of all children to the women included in the study were infected (Figure 1).

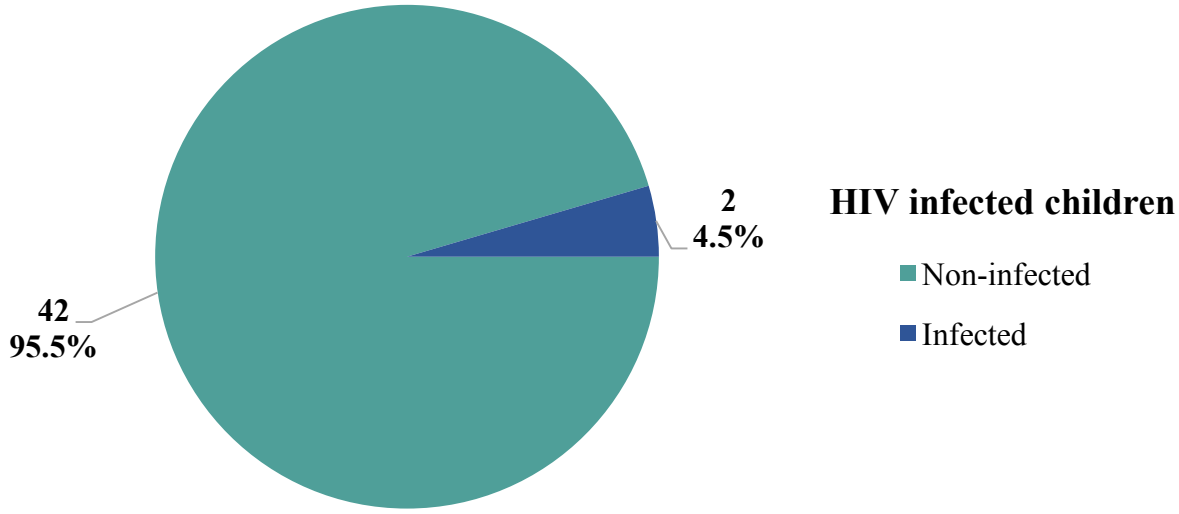

Figure 1. Proportions of HIV infected children among the children to the women included in the study. The numbers are number of children.

Almost all (20/21) participants were on first-line therapy and the most common therapy was TLE (Tenofovir, Lamivudine, Efavirenz), only one patient was on second-line therapy. Resistance-testing was not done in any patient. Side-effects were reported in eight of the participants. Lack of energy and abnormal sensation were the most common side-effects. CD4-levels were collected in 11/21 of the patients and the median level was 500 cells/µL. Viral loads were also available in 11/21 of the participants and nine of those had undetectable viral levels.

7.3 Adherence to ART

Nineteen women were adherent to their medication during the previous week (Figure 2). The women on both first- and second-line therapy had seven doses per week. For the two women with sub-optimal adherence, the reasons for sub-optimal adherence were “ran out of pills” and “had no food”.

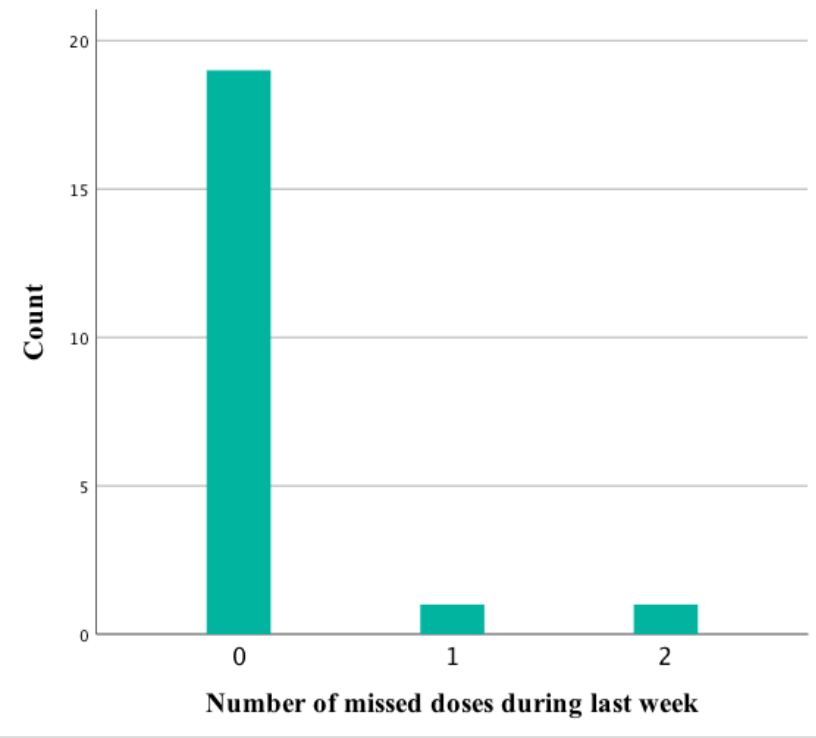

Figure 2. Number of missed doses during last week. All women were prescribed one dose per day (seven doses per week). Two women had sub-optimal adherence (one and two missed doses).

7.4 PARTICIPATION IN PMTCT PROGRAMME

CURRENT PARTICIPATION

The vast majority (18/21) of the women were within the first year after childbirth and 11/21 were already on ART when they became pregnant (Table 2). Median time since last delivery was 44 days and 11/21 of the women were attending PMTCT in addition to CTC.

Table 2. Current participation in PMTCT programme – characteristics.

Pregnancy status	First year after delivery	18 (86)
	Pregnant	2 (9)
	I don't know	1 (5)
PMTCT alone or in addition to another clinic	PMCTC and CTC	11 (52)
	PMTCT alone	8 (38)
	PMTCT and antenatal clinic	2 (10)
ART when became pregnant	Yes	11 (52)
	No (started in week XX *) **Median gestational week of starting with ART*	10 (48) 16

Data given as numbers (%).

PREVIOUS PARTICIPATION

Eight women had previously participated in a PMTCT programme and among those, two had ended prematurely (Figure 3). The reasons for ending prematurely were “My partner was sick” and “I lost the pregnancy”. Among the eight women with previous participation, four had participated more than one time before (one missing value).

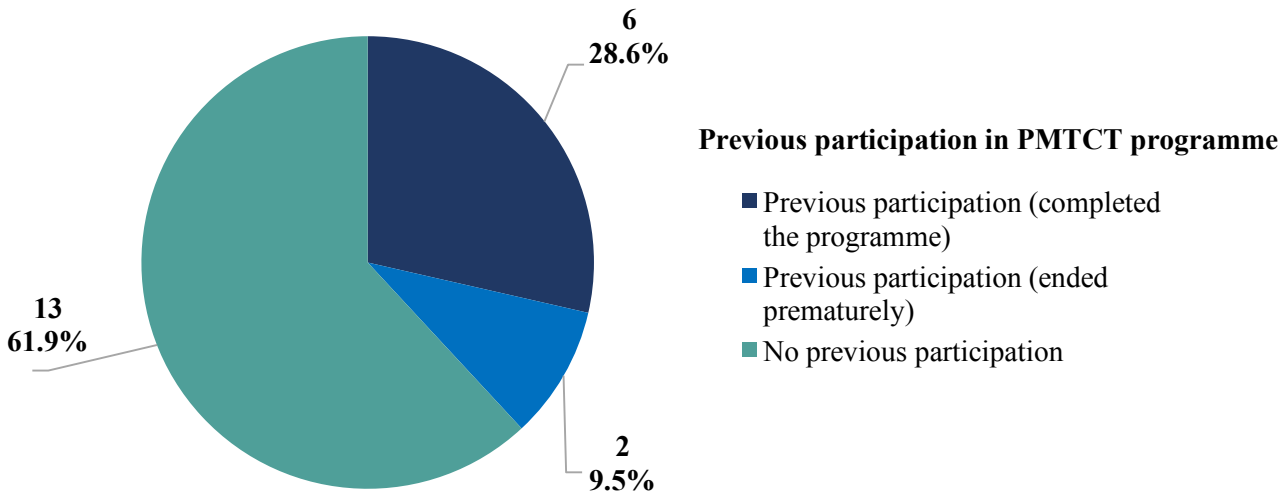

Figure 3. Proportions of previous participation in a PMTCT programme among the women attending the current PMTCT programme. The numbers are number of women.

There was no significant difference in ART adherence among women participating in the PMTCT programme for the first time (no previous participation) compared to those who had participated before (p = 0.51) (Table 3). The two women with sub-optimal adherence had not participated in a PMTCT programme before.

Table 3. Previous participation and adherence. Good adherence was considered to be an intake of 95% or more of the doses during the previous week.

		Adherence		Total
		Adherent	Non-adherent	
Previous participation	Count	8	0	8
	%	100%	0%	100%
No previous participation	Count	11	2	13
	%	84.6%	15.4%	100%
Total	Count	19	2	21
	%	90.5%	9.5%	100%

*P-value 0.51

Likewise, there was no significant difference in the HIV status of the children among mothers participating in the PMTCT programme for the first time compared to those who had participated before ($p = 1.00$).

7.5 Knowledge of ART and PMTCT programmes

The knowledge of ART and PMTCT programmes was in general good. Almost all women (20/21) knew that they are supposed to take their medication lifelong and 12/21 of the women knew that HIV can be transmitted from mother to child during both pregnancy, delivery, and breastfeeding. The majority (20/21) of women knew that a newborn infant should receive exclusive breastfeeding, furthermore two women also thought that warm water or porridge were suitable feedings.

The overall knowledge of each woman was analysed by reconstructing the three questions examining the knowledge of ART and PMTCT programmes to three new variables with only correct/wrong answers. The woman's knowledge was considered good if two thirds of the questions were answered correctly. According to this definition 19/21 of the women had good knowledge of ART and PMTCT programmes. The majority (19/21) of the women wanted to learn more in the PMTCT programme. The areas in which the women especially wanted more information in the PMTCT programme were HIV treatment and AIDS, education about HIV, and breastfeeding.

8. DISCUSSION

8.1 FINDINGS

PRIMARY FINDINGS

Participation in a PMTCT programme has been offered to all pregnant women with HIV in Moshi, Tanzania since 2004, but the outcome of the programme has previously not been evaluated. One of the main findings of this study is that 19/21 of the women (90%) coming for follow up in the PMTCT programme reported that they were adherent to their treatment during the last week, which is a very good number compared to previous studies. One study from Malawi in 2016 found that 73% of the pregnant women and 66% of the post-partum women were adherent. They used a different definition of adherence than we did. Adherence was defined as percentage of days the women followed their medical prescription (between clinical visits and with set time intervals of 3 months and 2 years) and good adherence was defined as > 90% of the days (37). In a study from Zambia in 2015, 83% of the pregnant women and 82% of the women six weeks post-partum were adherent. The definition for adherence they used was more similar to ours. They defined non-adherence as missing a drug or not following the medical prescription during the last four days (38). The different definitions of adherence used in studies makes it difficult to directly compare them with each other, but the self-reported adherence in our small population was very good. Generally, it has been shown that there is a higher risk of sub-optimal adherence during the post-partum period compared to non-pregnant and non-post-partum periods in a woman's life (39).

One problem with using self-reported adherence is that the percentage of participants with good adherence may be overestimated. Only half of the women in our study had a documented viral load and the date of the test was not known, so we cannot compare the self-reported adherence to

viral loads. Two participants had elevated viral loads, but since we do not know the date we do not know if it was during pregnancy or not. In another study from Tanzania it was shown that many mothers do not disclose suboptimal adherence until they are confronted with their viral loads (40).

We also found that only eight women had participated in a PMTCT programme before, a number which was surprisingly low considering that 15/21 of them had children prior the participation in the current PMTCT programme. One explanation for this could be that many women attending the PMTCT programmes in Pasua and KCMC are unaware of their attendance in the programme making it hard for them to remember previous participations. The reason for this is that since 2013, all pregnant and breastfeeding women are on lifelong ART and regular follow ups which makes the conversion from attendance in their regular HIV clinic to the PMTCT clinic more unnoticed.

Adherence and previous participation in PMTCT programmes

Our hypothesis was that women with previous participation in PMTCT programmes would have better adherence since they may have increased knowledge about HIV and HIV prevention than women attending the PMTCT programme for the first time. Surprisingly, we did not find a significant difference in ART adherence between women with previous PMTCT participation compared to women without. The small sample size is most likely one reason for this. Another explanation could be that information about HIV and the importance of adherence to lifelong ART has increased in the general population. Also, the unawareness of the conversion to a PMTCT programme mentioned above may be one reason. To our knowledge, there are no published data on this specific issue with ART adherence among women with previous PMTCT participation compared to women without.

Unfortunately, we did not have information on how many women that did not turn up at their PMTCT visits, or the reason for them not coming to their visits. The clinics do not have a list of patients so the doctors do not know how many patients are supposed to attend each day. One reason for non-attendance may be that their ART adherence is sub-optimal and that they do not want to reveal this to the doctor. This is one of the limitations with the study.

Among the eight women who had participated in a PMTCT programme before, six women (75%) completed the entire programme. In a meta-analysis from 2017, the rate of retention to care among women attending PMTCT programmes was less than rates among adults in general (41). Another study found that nearly 50% of the women initiating ART during pregnancy had missed a visit or were lost to follow up from the clinic six months postpartum (42). In Nigeria, only 66% of the women entering PMTCT programmes completed the programme with antenatal care, delivery services, and infant follow-up (43). Potential causes for the reasonably high percentage of completion in my study are; long time since the previous PMTCT programme makes it hard to remember completion/non-completion, the patient does not want to admit that she ended prematurely, and an answer from just one patient can affect the percentage a lot with this small sample size. Since only two women ended their PMTCT participation prematurely, no risk-factors for non-completion could be analysed. In addition, one of the women who ended prematurely did so because she "lost the pregnancy" which is not a "true" drop out, making the number of women completing the entire PMTCT programme even higher.

HIV STATUS OF THE CHILDREN

Two of the women had an HIV infected child and 2/44 (4.5%) of the children to all women were infected. There was no difference in HIV status of the children among women with previous or first participation in the PMTCT programme. In one study, the percentage of HIV infected infants

was 3% among women attending PMTCT care during antenatal or delivery periods and 20% among those who did not attend (43). This is comparable to another study where 2% of the infants to women attending PMTCT care were infected at the end of the PMTCT programme (44). Since the HIV status of the newborn infants was not known in this study, we cannot compare the numbers with previous studies.

Sociodemographic factors and knowledge of ART and PMTCT programmes

A high number (19/21) had good knowledge of ART and PMTCT programmes. This high number is an indication of a successful way of teaching this patient group about ART and PMTCT programmes in the health centres. Since there were only two women with suboptimal adherence we could not do any estimations of correlation between adherence and the following variables: education level, age, occupation, and knowledge of ART and PMTCT programmes. But current research about adherence to ART have showed some correlations between adherence and these variables. For example, a systematic review demonstrated that sub-optimal knowledge of HIV, ART, and PMTCT among pregnant and post-partum women were associated with lesser initiation, adherence, and retention to care (28). In addition, a study from Ghana showed that women with sub-optimal knowledge of ART and PMTCT had a higher risk of poor adherence to ART (27). Some previous studies have also shown that young age is a risk factor of sub-optimal ART adherence (37, 45). Lower education level has also been shown to be a risk factor for sub-optimal ART adherence (46).

8.2 Methodological considerations

We constructed a semi-structured questionnaire since this would be an adequate way of answering the hypothesis of my master thesis. Unfortunately, many obstacles occurred during the field study. One of the major complications was that my ethical application was denied so I could not participate in the distribution of the questionnaires. Consequently, patients and interviewers

could not ask me directly what I meant if there were any complicated questions even though we went through all questions carefully prior to initiation of the study. Due to the denial of the ethical approval the start of the field study was delayed for three weeks leading to a small sample size and in addition, the number of enrolled patients each week was less than expected. We had calculated in including a minimum of 50 participants, but ended up with 21. This is of course the biggest weakness with the study. If we had managed to include 92 women in this study we would have been able to see a difference between women with good adherence with previous participation in a PMTCT programme compared to women with good adherence with no previous participation (power = 0.8 and p-value < 0.05).

In addition, a few misinterpretations concerning some questions in the questionnaire was revealed during the second week leading to exclusion of these questions. Question number 17, 20, 23, 34, and question number 2 and 3 in "Information gathered from medical charts" were excluded (see Appendices, "Mothers interview questionnaire"). Other limitations of the study were that there were two interviewers and that the study took place in two health centres making the settings of filling in the questionnaires diverse.

The strengths of this study were that information was collected direct from the mothers, that the mothers could ask the interviewer if they had problems understanding the questions, and that the collected data was rather homogenous.

8.3 Further research

The two women with sub-optimal adherence had not participated in a PMTCT programme before, but no significant correlation between ART adherence and previous participation in a PMTCT programme was found. To test my hypothesis more appropriately and possibly receive a significant correlation in future studies, the number of participants must be greater. If an

additional hospital was included or the length of the study was increased, this could have been achieved. Furthermore, the questionnaire should be tested with some patients before it is used in the actual study.

During this study, questions and new aims were created. Firstly, it would be interesting to investigate if there are other factors that affect ART adherence among women attending the PMTCT programme in Moshi. For example, one could investigate if other diseases among the women affect ART adherence and if there are any differences between the health clinics. Since we could not receive any information on the number of women that did not turn up at their PMTCT visits, it would be interesting to receive data on this and their reason for non-attendance. Another question that would be interesting to investigate is how the adherence to ART differs if you do a study using pill-count instead of self-reported adherence.

9. CONCLUSIONS

One of the main conclusions of this study was that adherence rate among the women attending the PMTCT programme in Pasua health centre and KCMC, in Moshi, Tanzania, is high. Also, women attending the PMTCT programme in Pasua Health centre and KCMC, have good knowledge of ART and PMTCT programmes. No correlation between previous participation in PMTCT programme and ART adherence was found. Neither, no significant difference on the child's/children's HIV status between mothers with previous participation in PMTCT programmes compared to mothers with no previous participation was found.

Since the number of participants in this study was low, no general conclusions can be drawn from these results. Nonetheless, the results can be used to create new aims for further research on ART adherence among women attending PMTCT programme.

Since the adherence rate and knowledge of ART and PMTCT programmes in Moshi is high, several actions have already been done for this patient group. To improve the adherence to ART and further decrease the MTCT, several actions can be done. Since 19/21 of the women wanted to learn more in the PMTCT programme, there are great opportunities to increase knowledge in this patient group. Increased knowledge may lead to increased ART adherence and decrease stigma in the society. Furthermore, nearly half of the women were not on ART when they became pregnant and of those the median gestational week of starting with ART was week 16. This could be improved by increased knowledge among the women to make them come to ANC directly when they know they are pregnant and take a HIV test.

10. POPULÄRVETENSKAPLIG SAMMANFATTNING PÅ SVENSKA

Hög följsamhet till HIV-medicinering bland HIV-positiva kvinnor i norra Tanzania

Globalt sett är HIV/AIDS en av huvudorsakerna till dödlighet bland kvinnor i reproduktiv ålder. För att förhindra att HIV-infektionen förs över till barnet är det viktigt att mammorna har hög följsamhet till sin HIV-medicinering då låga, icke-mätbara virusnivåer drastiskt minskar risken för överföring under graviditet, förlossning och amning. Det är viktigt att ha kunskap kring kvinnors följsamhet till HIV-medicinering för att sjukvården ska kunna sätta in riktade åtgärder.

För att undersöka detta gjordes en studie på två HIV-kliniker i Moshi i norra Tanzania. Studien gick ut på att undersöka om kvinnor som lever med HIV och tidigare har deltagit i ett program för att förhindra överföring av HIV till sitt barn (PMTCT program), har bättre följsamhet till sin HIV-medicinering än kvinnor som inte har deltagit i detta program tidigare. Med följsamhet menas att patienten följer ordinationen och tar rätt mediciner vid rätt tidpunkt. Definitionen på god följsamhet är vedertagen och innebar att minst 95% av doserna skulle ha intagits under föregående vecka. Mammorna intervjuades med hjälp av en enkät och journalinformation samlades in som komplement.

Tjugoen kvinnor deltog i studien varav nitton (90%) hade god följsamhet till sin HIV-medicinering. De två kvinnor som hade bristfällig följsamhet angav ”medicinen tog slut” och ”hade ingen mat” som anledningar till bristande följsamhet. Åtta kvinnor (38%) hade deltagit i ett PMTCT program tidigare och av dessa hade två kvinnor avbrutit programmet i förtid.

Slutsatserna man kan dra av denna studie är att följsamheten till HIV-medicinering bland HIV-positiva kvinnor i Moshi är hög. Kvinnor som tidigare hade deltagit i ett PMTCT program hade inte bättre följsamhet till sin HIV-medicinering än kvinnor som deltog för första gången. Dock

var antalet patienter som deltog i studien lågt och det är möjligt att man skulle fått andra resultat om antalet patienter hade varit högre.

Resultaten i denna studie kan användas för att skapa nya frågeställningar till framtida studier på denna patientgrupp. Ökad kunskap kring kvinnors följsamhet till HIV-medicinering är viktigt för att kunna sätta in riktade åtgärder, öka följsamhet till HIV-medicinering och på så sätt kunna minska risken för överföring av HIV från mamma till barn.

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12. REFERENCES

1. UNAIDS. Global Factsheets 2016: UNAIDS; 2016 [2018-02-02]. Available from: http://aidsinfo.unaids.org/.
2. World Health Organization. New WHO recommendations: Preventing mother-to-child transmission http://www.who.int/hiv/pub/mtct/en/2009 [2018-01-26]. Available from: http://www.who.int/hiv/pub/mtct/mtct_key_mess.pdf.
3. World Health Organization. Global Health Observatory (GHO) data: HIV/AIDS: WHO; 2016 [2018-01-26]. Available from: http://www.who.int/gho/hiv/en/.
4. The World Bank. Tanzania Country Profile 2016, : The World Bank; 2016 [2017-08-26]. Available from: http://data.worldbank.org/country/tanzania?view=chart
5. Ministry of Health and Social Welfare Tanzania. National guidelines for the management of HIV and AIDS. Fifth ed: Ministry of Health and Social Welfare Tanzania; 2015. p. 103-24.
6. UNAIDS. Country factsheets, United republic of Tanzania 2016: UNAIDS; 2016 [2018-01-26]. Available from: http://aidsinfo.unaids.org/.
7. Gisslén M. HIV och AIDS. In: Iwarson S, editor. Infektionsmedicin. Sixth ed: Säve förlag; 2014. p. 241-52.
8. World Health Organization. Mother-to-child transmission of HIV 2017 [2017-09-15]. Available from: http://www.who.int/hiv/topics/mtct/about/en/.
9. Gisslén M. HIV och graviditet, internetmedicin.se, 2017 [updated 2017-07-03, 2017-08-27]. Available from: http://www.internetmedicin.se/page.aspx?id=1710.
10. Referensgruppen för AntiViral terapi. Profylax och behandling av hivinfektion vid graviditet, 2017: RAV; 2017 [2018-05-08]. Available from: http://www.sls.se/globalassets/rav/rekommendationer/hiv-gravida_final-20171207.pdf.
11. World Health Organization. Guideline: updates on HIV and infant feeding: the duration of breastfeeding, and support from health services to improve feeding practices among mothers living with HIV: WHO; 2016 [2018-01-29]. p. 6]. Available from: http://apps.who.int/iris/bitstream/10665/246260/1/9789241549707-eng.pdf?ua=1.
12. European Collaborative Study. Risk factors for mother-to-child transmission of HIV-1. Lancet (London, England). 1992;339(8800):1007-12.
13. Mandelbrot L, Mayaux MJ, Bongain A, Berrebi A, Moudoub-Jeanpetit Y, Benifla JL, et al. Obstetric factors and mother-to-child transmission of human immunodeficiency virus type 1: the French perinatal cohorts. SEROGEST French Pediatric HIV Infection Study Group. American journal of obstetrics and gynecology. 1996;175(3 Pt 1):661-7.
14. Landesman SH, Kalish LA, Burns DN, Minkoff H, Fox HE, Zorrilla C, et al. Obstetrical factors and the transmission of human immunodeficiency virus type 1 from mother to child. The Women and Infants Transmission Study. The New England journal of medicine. 1996;334(25):1617-23.
15. Mofenson LM, Lambert JS, Stiehm ER, Bethel J, Meyer WA, 3rd, Whitehouse J, et al. Risk factors for perinatal transmission of human immunodeficiency virus type 1 in women treated with zidovudine. Pediatric AIDS Clinical Trials Group Study 185 Team. The New England journal of medicine. 1999;341(6):385-93.
16. European Collaborative Study. Mother-to-child transmission of HIV infection in the era of highly active antiretroviral therapy. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2005;40(3):458-65.
17. White AB, Mirjahangir JF, Horvath H, Anglemyer A, Read JS. Antiretroviral interventions for preventing breast milk transmission of HIV. The Cochrane database of systematic reviews. 2014(10):Cd011323.
18. John GC, Nduati RW, Mbori-Ngacha DA, Richardson BA, Panteleeff D, Mwatha A, et al. Correlates of mother-to-child human immunodeficiency virus type 1 (HIV-1) transmission:

association with maternal plasma HIV-1 RNA load, genital HIV-1 DNA shedding, and breast infections. The Journal of infectious diseases. 2001;183(2):206-12.
19. Embree JE, Njenga S, Datta P, Nagelkerke NJ, Ndinya-Achola JO, Mohammed Z, et al. Risk factors for postnatal mother-child transmission of HIV-1. AIDS (London, England). 2000;14(16):2535-41.
20. World Health Organization. HIV/AIDS - Treatment and care WHO; [2018-02-05]. Available from: http://www.who.int/hiv/topics/treatment/en/.
21. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach – 2nd ed: WHO; 2016 [2018-02-09]. Available from: http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684_eng.pdf?ua=1.
22. Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, Squier C, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Annals of internal medicine. 2000;133(1):21-30.
23. Bezabhe WM, Chalmers L, Bereznicki LR, Peterson GM. Adherence to Antiretroviral Therapy and Virologic Failure: A Meta-Analysis. Medicine. 2016;95(15):e3361.
24. Mmiro FA, Aizire J, Mwatha AK, Eshleman SH, Donnell D, Fowler MG, et al. Predictors of early and late mother-to-child transmission of HIV in a breastfeeding population: HIV Network for Prevention Trials 012 experience, Kampala, Uganda. Journal of acquired immune deficiency syndromes (1999). 2009;52(1):32-9.
25. Nachega JB, Uthman OA, Anderson J, Peltzer K, Wampold S, Cotton MF, et al. Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: a systematic review and meta-analysis. AIDS (London, England). 2012;26(16):2039-52.
26. Ekama SO, Herbertson EC, Addeh EJ, Gab-Okafor CV, Onwujekwe DI, Tayo F, et al. Pattern and determinants of antiretroviral drug adherence among Nigerian pregnant women. Journal of pregnancy. 2012;2012:851810. 2017/09/16
27. Boateng D, Kwapong GD, Agyei-Baffour P. Knowledge, perception about antiretroviral therapy (ART) and prevention of mother-to-child-transmission (PMTCT) and adherence to ART among HIV positive women in the Ashanti Region, Ghana: a cross-sectional study. BMC women's health. 2013;13:2.
28. Hodgson I, Plummer ML, Konopka SN, Colvin CJ, Jonas E, Albertini J, et al. A systematic review of individual and contextual factors affecting ART initiation, adherence, and retention for HIV-infected pregnant and postpartum women. PloS one. 2014;9(11):e111421.
29. The United States President's emergency plan for aids relief (PEPFAR). Tanzania Country Operational Plan (COP) 2015 Strategic Direction Summary: United States Department of State; 2015 [2018-02-22]. Available from: https://www.pepfar.gov/documents/organization/250304.pdf.
30. World Health Organization. Consolidated guidelines on the use of Antiretroviral drugs for treating and preventing HIV infection: WHO; 2013 [2018-02-22]. Available from: http://www.who.int/hiv/pub/guidelines/arv2013/download/en.
31. Ministry of Health Cd, gender, eldery, and children in Tanzania. Chart: Percentage of pregnant women who received counseling on HIV, had an HIV test during ANC, and received the results - MOH Tanzania 2017 [2018-02-26]. Available from: https://hmisportal.moh.go.tz/hmisportal/ -/indicator/pmtct.
32. Kilimanjaro Christian Medical Centre (KCMC). Care and treatment clinic (CTC) & Child centred family care clinic (CCFCC) [2018-02-26]. Available from: https://www.kcmc.ac.tz/index.php?q=ctc.
33. Rune Philemon. Personal communication, 2018-02-23. In: Jönsson L, editor.
34. Ministry of Health CD, Gender, Elderly and Children (MoHCDGEC) [Tanzania Mainland], Ministry of Health (MoH) [Zanzibar], National Bureau of Statistics (NBS), Office of the Chief

Government Statistician (OCGS), and ICF. 2016. Tanzania Demographic and Health Survey and Malaria Indicator Survey 2015-2016. 2016.
35. Ministry of Health CD, Gender, Elderly and Children. National guidelines for the management of HIV and AIDS. Sixth ed. Dar es Salaam, 2017.
36. UNESCO Office Dakar and Regional Bureau for Education in Africa UODeS, Tanzania UR, Ministry of Education and Vocational Training, Pôle de Dakar. Tanzania education sector analysis: beyond primary education, the quest for balanced and efficient policy choices for human development and economic growth 2012 [2018-05-29]. Available from: http://unesdoc.unesco.org/images/0021/002152/215247e.pdf.
37. Haas AD, Msukwa MT, Egger M, Tenthani L, Tweya H, Jahn A, et al. Adherence to Antiretroviral Therapy During and After Pregnancy: Cohort Study on Women Receiving Care in Malawi's Option B+ Program. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2016;63(9):1227-35.
38. Okawa S, Chirwa M, Ishikawa N, Kapyata H, Msiska CY, Syakantu G, et al. Longitudinal adherence to antiretroviral drugs for preventing mother-to-child transmission of HIV in Zambia. BMC pregnancy and childbirth. 2015;15:258.
39. Henegar CE, Westreich DJ, Maskew M, Miller WC, Brookhart MA, Van Rie A. Effect of pregnancy and the postpartum period on adherence to antiretroviral therapy among HIV-infected women established on treatment. Journal of acquired immune deficiency syndromes (1999). 2015;68(4):477-80.
40. Ngarina M, Popenoe R, Kilewo C, Biberfeld G, Ekstrom AM. Reasons for poor adherence to antiretroviral therapy postnatally in HIV-1 infected women treated for their own health: experiences from the Mitra Plus study in Tanzania. BMC public health. 2013;13:450.
41. Knettel BA, Cichowitz C, Ngocho JS, Knippler ET, Chumba LN, Mmbaga BT, et al. Retention in HIV Care During Pregnancy and the Postpartum Period in the Option B+ Era: A Systematic Review and Meta-Analysis of Studies in Africa. Journal of acquired immune deficiency syndromes (1999). 2017.
42. Phillips T, Thebus E, Bekker LG, McIntyre J, Abrams EJ, Myer L. Disengagement of HIV-positive pregnant and postpartum women from antiretroviral therapy services: a cohort study. Journal of the International AIDS Society. 2014;17:19242.
43. Rawizza HE, Chang CA, Chaplin B, Ahmed IA, Meloni ST, Oyebode T, et al. Loss to Follow-Up within the Prevention of Mother-to-Child Transmission Care Cascade in a Large ART Program in Nigeria. Current HIV research. 2015;13(3):201-9.
44. Kyaw KWY, Oo MM, Kyaw NTT, Phyo KH, Aung TK, Mya T, et al. Low mother-to-child HIV transmission rate but high loss-to-follow-up among mothers and babies in Mandalay, Myanmar; a cohort study. PloS one. 2017;12(9):e0184426.
45. Erlwanger AS, Joseph J, Gotora T, Muzunze B, Orne-Gliemann J, Mukungunugwa S, et al. Patterns of HIV Care Clinic Attendance and Adherence to Antiretroviral Therapy Among Pregnant and Breastfeeding Women Living With HIV in the Context of Option B+ in Zimbabwe. Journal of acquired immune deficiency syndromes (1999). 2017;75 Suppl 2:S198-s206. 2017/09/16
46. Ayuo P, Musick B, Liu H, Braitstein P, Nyandiko W, Otieno-Nyunya B, et al. Frequency and factors associated with adherence to and completion of combination antiretroviral therapy for prevention of mother to child transmission in western Kenya. Journal of the International AIDS Society. 2013;16:17994.

13. APPENDICES

MOTHERS INTERVIEW QUESTIONNAIRE		
QUESTIONNAIRE NUMBER		
STUDY ID NUMBER		
STUDY SITE		
DATE OF ENROLMENT		
CLIENT NUMBER		
GENERAL INFORMATION		
1. Mothers date of birth		
2. Occupation		Employed
		House wife
		Self employed
		Student
		Retired
		Other
3. Level of education		Never been to school
		Finished primary education
		Not finished primary education
		Secondary school for 4 years
		Secondary school for 6 years
		Vocational college
		University
4. Marital status		Married
		Single
		Cohabiting
		Separated
		Divorced
		Widow
5. Residence		Village
		Urban
6. Religion		Muslim
		Catholic
		Protestant
		Pagan/none
		Other religion
7. Time to reach facility from home	(in minutes):	
8. Means of transportation to getting to facility		Walking
		Motorcycle
		Bus
		Taxi
		Private car
		Other means of transportation

HISTORY OF HEALTH		
9. When were you diagnosed with HIV?		
10. How did you find out your status?		Tested at health facility
		Tested at VCT
		Tested at campaign
		Other
11. What drove you to get tested?		I was asked
		I asked to be tested
		My partner had been infected
		Routine testing at the clinic
		Part of PMTCT
		Other (please specify)
12. Pregnancy status		I am pregnant
		I was pregnant within the past year)
		I don't know
13. Number of living children		
14. Number of infected children		

PREVIOUS PMTCT ENCOUNTERS		
15. Have you participated in PMTCT previously?		Yes
		No
16. How many times have you participated in a PMTCT programme?		
17. Before your current pregnancy/delivery, when was the last time you participated in PMTCT?		
18. Did you stop PMTCT prematurely?		Yes, go to question 19
		No, skip question 19
19. If yes, why?		Didn't have time
		Far from home
		I didn't think it was a good program
		Fear of stigma
		Other
20. Since your last pregnancy, could you go on and use ARVs without stopping?		Yes
		No

CURRENT PARTICIPATION IN PMTCT PROGRAMME			
21. When did you start PMTCT for the current pregnancy?	Month		Year
22. Do you have a clinic for PMTCT only or in addition to another clinic?		PMTCT only	
		PMTCT and antenatal clinic	
		PMTCT and CTC	
		PMTCT and others	

23. Since you started the current PMTCT programme, how many times have you attended?	

ANTIRETROVIRAL THERAPY		
24. What ARVs are you taking? (please, specify all of them)		
25. Date of starting current regimen		
26. In the past week, how many times did you miss your medication?		
27. If you have missed any medication, what was the reason? (Multiple answers are possible)		I ran out of pills
		Forgot/left medicines at home
		I had a lot of medication to take
		I was afraid of side effects
		I was sick
		Couldn't afford it
		I didn't want anyone to see me taking the drugs
		Other (please specify)
28. Were you on ARV when you got pregnant? If no, when during pregnancy did you start?		I was on treatment when I got pregnant.
		No, I started when I was in week _____ of my pregnancy
29. Were you on ARV during your last breastfeeding period?		No, none at all
		Yes, every day
		Yes, part of the time during breastfeeding

SIDE-EFFECTS		
30. Have you experienced any side-effects of the ARVs?		Lack of energy
		Myalgia
		Skin disease
		Insomnia
		Loss of appetite
		Depression
		Loss of libido
		Diarrhea
		Headache
		Skin rash
		Losing weight
		Anaesthesia/abnormal sensation
		Others (please specify)
		None

BREASTFEEDING		
31. Date of last delivery?		
32. Did you breastfeed after delivery?		Yes

		No, (If you answered "No", please go to question 36)
		This is my first pregnancy (If you answered, “This is my first pregnancy”, please go to question 36)
33. If you answered "Yes", for how long did you breastfeed? (Please specify in months)		
34. If you answered “Yes”, can you specify the duration of exclusive breastfeeding and the duration of breastfeeding in total after your previous delivery?		Exclusive breastfeeding (in months)_____
		Breastfeeding in total (in months)_____
35. If you answered "Yes", was the baby tested for HIV after you finished breastfeeding?		Yes
		No
		Still breastfeeding

KNOWLEDGE OF ANTIRETROVIRAL THERAPY AND PMTCT PROGRAMMES		
36. For how long do you think you have to take your HIV drugs? (choose one option)		2 months
		2 years
		Life long
		Until I have no symptoms/ my health is good
		As long as the doctor tells me
		I don’t know
		Other (please specify)
37. What more would you like to see being done at PMTCT programme? (you can choose more than one option)		Information/ message about treatments and effects of AIDS
		Family planning counselling
		Education about HIV and AIDS
		Information about pregnancy
		Information about delivery
		Care of an infant with HIV
		Information on how to breastfeed
		How to deal with those who stigmatise me
		Other (please specify)
38. When can HIV be transmitted from mother to child? (You can choose more than one option)		During pregnancy
		By sharing bottled water
		During breastfeeding
		During changing diapers
		During delivery
39. If you have taken your ARV and you have a very small child, how will you		Exclusive breastfeeding
		Alternative feeds

feed the child? (You can choose more than one option)		Alternative milk
		Solid food
		Others (please specify)

Information gathered from medical charts:				
1. Immune status of the mother:				
Most recent CD4				
Viral load				
Has any resistance testing been performed?		Yes		No
2. Previous participation in PMTCT programme - last time				
ART prophylaxis		Yes		No
ART prophylaxis during delivery		Yes		No
ART prophylaxis during breastfeeding		Yes		No
3. Previous participation in PMTCT programme – last time (if possible)				
Duration		Completed program		
		Ended prematurely		
Number of visits during pregnancy				
4. HIV status of Children				
Number of HIV positive children if possible				