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Factors contributing to viral load suppression amongst pregnant & breastfeeding women on ART in Lesotho

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RESEARCH REPORT

Factors contributing to viral load suppression amongst pregnant & breastfeeding women on ART in Lesotho

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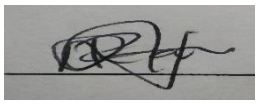
School of Public Health, Faculty of Health Sciences University of the Witwatersrand, Johannesburg

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree Master of Science in Epidemiology in the Field of Population-Based Field Epidemiology

Declaration

I, Puseletso Maja (1606115) affirm the report to reflect my efforts. This submission is for fulfilment of my Master in Public Health (Maternal and Child Health) under the School of Public Health in the University of Witwatersrand. I also reaffirm that the report has not been submitted under any university for completion of any degree. I have also adhered to referencing conventions and acknowledged appropriately to cite people's thoughts, findings and ideas.

Signature: 

Date: 19 March 2021

Dedication

I dedicate the report to all the unborn babies who will be born HIV free due to policy shifts made in Lesotho to support their HIV positive pregnant and breastfeeding mothers.

ABSTRACT

Background

Despite Lesotho achieving ANC ART coverage of >90%, mother to child transmission rate at 9% in 2019. The aim of the study was therefore, to describe factors contributing to viral load suppression amongst HIV infected pregnant and breast-feeding women in Maseru and association of maternal viral load suppression to infant DNA PCR positivity in Maseru, Lesotho.

Methodology

A descriptive, cross-sectional study on HIV positive pregnant and breastfeeding women using secondary data analysis was employed to identify patients' files and cards so as to retrieve detailed information. At bivariate analysis level was used to assess the existence of associations between different exposures and virological suppression. Multivariate analysis conditional logistic regression model with virological suppression as the response variable.

Results

Two thousand two hundred and sixty-six (94.7%) of those breastfeeding and 492 (96.1%) of those pregnant were virally suppressed. Marital status, age and partner's HIV status were socio-demographic variables that were statistically associated with viral load suppression. Duration of ART, adherence (%) and completion, ever defaulted, transfer in from other facilities, total drugs taken and dosage, knowledge of HIV status timing and type of regimen all were statistically associated with viral load.

Women aged above 25 were more likely to be virally suppressed than those below 25 years. Women whose partner's HIV status was known were respectively 4.8 (95% CI 1.9-11.9) for negative status and 4.1 (95% CI 2.1-7.7) for positive status times more likely to be viral load suppressed than those with partners of unknown status. Transfer in and women who knew their HIV status during pregnancy were more likely to be virally suppressed. This study has also shown that the higher the VL the higher the risk of HIV transmission.

Conclusion and Recommendations

Lack of viral load suppression in some women is concerning and signifies a threat to the aim of eliminating mother to child transmission in the country. Lesotho can intensify support provided by VHW's and peer support groups to postpartum women to improve their adherence and improve their viral load suppression. Women who have been on ART prior to their pregnancy should also receive intensified counselling emphasizing on MTCT as knowledge enhances adherence. Lesotho has to adopt a one-month viral load monitoring interval after the 1st encounter of high viral load in pregnant and breast-feeding women for prompt decision making in management.

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Abbreviations

ART (Antiretroviral transmission)

PMTCT (Prevention of Mother to Child Transmission)

MTCT (Mother to Child Transmission)

HIV (Human Immunodeficiency Virus)

AIDS (Acquired Immunodeficiency Syndrome)

VL (Viral Load)

EID (Early Infant Diagnosis)

EMTCT (Elimination of Mother to Child Transmission)

ANC (Antenatal Care)

CD 4 (Cluster of differentiation 4)

MOH (Lesotho Ministry of Health)

WHO (World Health Organization)

AZT (Zidovudine)

NVP (Nevirapine)

NNRTI (Non-nucleoside reverse transcriptase inhibitors)

DNA-PCR (DNA Polymerase chain reaction)

Chapter 1: Introduction and Literature Review

1.1 Background

HIV is a critical global health pandemic and has existed for a long time. Despite ARVs being adapted to reduce their toxicity and simplify dosing, an HIV cure still remains unknown in the current decade (1). 37.9 million people were estimated to be HIV infected globally in 2018, with 1.7 million as children (2). The global HIV prevalence among adults aged 15-49 has reduced since 2001 and now at 0.7% in 2019 (3). The burden of HIV differs significantly within different regions globally. However, Sub-Saharan Africa has approximately 68% of its population infected with HIV (2) with HIV prevalence (15-49) of 6,7% in 2018 (4). Therefore, sub-Saharan Africa is the epicentre of the HIV pandemic.

Lesotho has the second highest HIV prevalence globally after Swaziland with 24.6% for those aged 15-49 years (5). Amongst pregnant women, HIV prevalence was at 26% in the 2013 ANC sentinel surveillance (6) and females of reproductive age 15-49 years at 29.4% (5). PMTCT services in Lesotho were officially launched in 2003 and implemented in 186 sites (7). As below, they evolved from providing a single dose regimen in 2003 to provision of lifetime ART for those tested HIV positive since 2014/15.

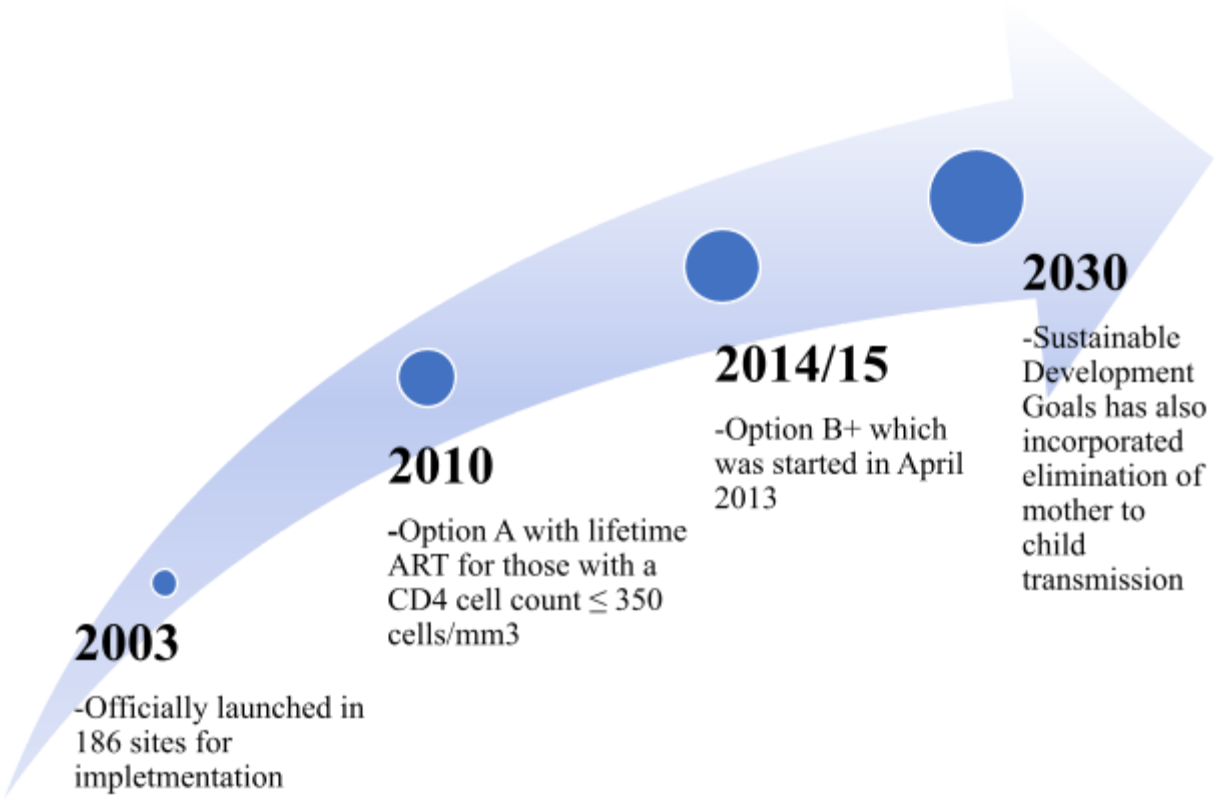


Figure 1: Prevention of mother to child transmission services in Lesotho

Without any treatment, 35–40% of children born from HIV-infected mothers can be in perinatally infected, during delivery, or during the period of breast-feeding (8). Approximately 15,000 women infected with HIV in Lesotho deliver each year (9). With no interventions in place to hinder vertical transmission, an estimated 5,900 of new paediatrics could be infected (9). In 2003, the United Nations approved a deliberate approach regarding prevention of mother to child transmission using a four-component strategy (10):

1. On HIV infection prevention primarily amongst child-bearing women (10);
2. Unplanned pregnancies prevention amongst women who are HIV infected (10);
3. Mother-to-child-Transmission (10);
4. Family centred approach for provision of appropriate HIV treatment and care amongst women (10).

WHO then adopted new guidelines in 2015 as Option B+ by expanding on the 4th component of the PMTCT strategy as mentioned above. It intended to provide ART despite the CD4 count or

clinical stage for every pregnant and breastfeeding woman who tests positive or is living with HIV (11). Therefore, this meant that more pregnant women can be placed on lifelong ART. This was aimed to eliminate new HIV infections amongst children (11).

Lesotho Ministry of Health (MOH), then began implementation of this new approach in April 2014/15 (9). Before the universal coverage of ART to all pregnant and breastfeeding, WHO had previously guided other approaches of PMTCT. In 2010, WHO recommendations for PMTCT had previously been on clinical and immunologic criteria for lifelong antiretroviral therapy (ART) where initiation was fast-tracked (12). This was adopted by Lesotho and introduced as Option A with lifetime ART for those with a CD4 cell count ≤ 350 cells/mm3 and NVP prophylaxis for six weeks for their infants (7) (13). In contrast, those not eligible were provided with AZT from 14 weeks' pregnancy and maternal NVP as a single dose at first signs of labour with infant ART prophylaxis (NVP) up until breastfeeding termination (14). Another recommendation in the same year was the arm of Option B arm that stated that all HIV positive pregnant and breastfeeding women should be started on a combined three-drug antiretroviral prophylaxis their entire antenatal phase until lactation cessation for those not eligible for lifelong ARVs (12). Current policy under PMTCT in Lesotho was adopted in 2014/15 which indicated that ART should be provided for all eligible women despite their CD4 count (9) as earlier alluded to.

According to WHO, viral load suppression should be attained within the first 6 months of being on ART (15). Therefore, where possible VL monitoring should be done to determine viral replication or confirm any failure to treatment (16). According to Lesotho guidelines, viral load monitoring should be done after 6 months of initial ART commencing and then 12 months later when virally suppressed for adult population(17). However, there are differences on how viral load is monitored between the adult population and pregnant and breastfeeding women on ART, as their viral load evaluation is monitored after every 6 months (17). This is for the purpose of identifying any treatment failure earlier to protect the foetus or a breastfeeding child from being HIV infected by their mother due to the high viral load.

Efforts have been put in place by the Joint United Nation Programme to end the AIDS epidemic by 2030 (18). This has propelled countries towards achieving the 90-90-90 targets (18). This target's goal is to diagnose 90% of unknown people living with HIV, offer 90% of those

identified HIV positive antiretroviral therapy (ART) and viral suppression to the 90% of those on ART by 2020 (18). Lesotho currently is at 87.7% of viral load suppression for the general HIV infected adult population (5). Nevertheless, specific viral load suppression data for pregnant and breastfeeding women on ART is still unknown. This is extremely crucial as countries seek to eliminate mother to child transmission (MTCT) (18). Knowledge of viral load suppression rate among pregnant and breastfeeding women, can assist in evaluating the PMTCT program for those who are already on ART. This will enable identification of gaps that hinder their adherence and in turn can cause elevated viral load among this population which poses challenges in progress towards elimination of mother to child transmission.

In July 2011, the Global Plan to eliminating new HIV infections amongst children by 2015 was launched during the high-level United Nations General Assembly meeting on AIDS in the New York city (19). Progress to reduce mother-to-child transmission of HIV has been significant since the global plan and largely scale up ART in pregnant women living with HIV has led to about a 52% decline of global new infections for under-5 children (20). This Elimination of mother to child transmission rate ranges as high as 26.6% in Indonesia to as low as 4.1% in Uganda (21). However, in Eastern and Southern Africa, where Lesotho is situated, the average rate of MTCT is at 9.9% (22). Nevertheless, Lesotho is still lagging behind with MTCT at 12.4% at final transmission with breast-feeding time and 6.94% at 6 weeks according to DHIS 2014 (23) whilst our neighboring country South Africa was at 1.4% in 2016 for final rate transmission (13). Progress has been noted under UNAIDS, reporting estimates of 6.2% at 6 weeks and 11.0% at final transmission rate in 2016 (24) and currently in 2020 with estimates of 6-week transmission rate at 5% with end of lactating period at 9%. (25). This shows that Lesotho is on the right track of reducing mother to child transmission but has still failed to achieve the <5% of final rate transmission which marks that as elimination of mother to child transmission for the country.

1.2 Problem Statement

Monitoring of individuals on ART is critical to attain viral load suppression with the growth of ART programme with initiations of all eligible people as the core value of ART to those infected is to reduce their viral load (26). The role of active ART use is prompt and persistent viral load suppression (27). This is more critical in pregnant and breast-feeding women so that mother to child transmission is prevented and overall maternal health is achieved. Intensifying access to (ART) for pregnant and postpartum women living with HIV in low and middle-income countries

has made a significant improvement in maternal health and reduction of mother to child transmission (28). HIV transmission rate is estimated at 5% or less when women take ART during pregnancy or breastfeeding period (21) and are virally suppressed. Lesotho national HIV estimates indicated that HIV 6 week rate transmission from mother to child declined from 5.9% in 2012 to 3.5% in 2014 (6). Similarly, PMTCT coverage has been stipulated to have declined from 89% in 2012 to 72% in 2014 and therefore emasculating progress previously made (6). In the UNAIDS 2016, Lesotho was estimated to range between 66-94% of PMTCT coverage with other low- and middle-income countries between 2010-2015 (20). However, UNAIDS 2018, stated that Lesotho is estimated to be amongst countries with >90% of positive pregnant women on ART (21), contrary to the coverage previously affirmed. Furthermore, new infections from mother to child transmission amplified from 1 700 in 2012 to 2 200 in 2014 (6). This can suggest that the problem in achieving elimination of mother to child transmission is not so much PMTCT ART coverage but rather suppression among those who are on ART.

Viral load monitoring is imperative in evaluating adequate adherence and any failure to treatment which would inform the next management steps and need to switch to the next regimen. There is a greater pill burden with second line regimens, which are more demanding and expensive to adhere in comparison to the first-line regimens (29). Therefore, factors contributing to viral suppression should be addressed as much as possible. According to Lesotho guidelines, the cut off for viral suppression is <1000 copies/ml (17). The higher the level of viral load in a pregnant mother's blood, the higher the risk of vertical transmission (30) despite being on ART if suppression is not attained. Amongst HIV infected people on ART in Lesotho, 87.7% had viral load suppression with younger people at 77.2% and those between 35-49 years of age at 89.9% (5).

Viral suppression amongst pregnant and breast-feeding women is still unknown in Lesotho. Despite the estimated high ART coverage amongst them (21), mother to child transmission persists to be high (23). This could mean that there are some pregnant and breastfeeding women on ART who are not virally suppressed resulting in the higher transmission rates reported.

1.3 Justification

Insufficient ART adherence is by far the most important cause of viral load non-suppression after a client has been on ART for 6 months (28, 31) due to inadequate plasma drug levels (32).

Clinical, virological and immunological success are dependent on optimal adherence, as the virus can rapidly acquire therapy-limiting drug resistance (33). Enhanced ART adherence is linked to improved virological effects in a direct dose-response pattern, hence an expected optimal adherence from each patient (34). The main mode of HIV transmission from mother to child globally is in the period of pregnancy, labour, delivery, and whilst breastfeeding (35) due to high viral load as earlier alluded to. Even though more than 90% of pregnant and breastfeeding women in Lesotho are on ART, many might still have high viral loads and therefore continue to transmit HIV. Correlation exists that, risk of transmitting HIV to an infant increases when a pregnant or breastfeeding mother has a higher level of HIV of about >1000 copies/ml in their blood or vagina during delivery (36). Similarly, factors associated with postnatal transmission risk through breastfeeding include high viral load and low CD 4 count of the mother (36). With continual risk of HIV transmission during breastfeeding period, effective adherence on ART for viral suppression is important during such periods (18). Factors that lead to or are associated with non-adherence vary considerably. They include psychosocial stressors which are increased due to the pregnancy itself or caregiving periods, existing side effects of ART or pill burden and insufficient counselling on achieving or maintaining VL suppression during breastfeeding (35). Furthermore, factors that facilitate or become barriers in adherence were categorized into three main groups (35). They are classified on the individual level, the community with their partners and health systems (35).). Factors affecting viral load suppression, specifically during pregnancy and breastfeeding, have not been assessed in Lesotho as a possible gap of why the country has not achieved elimination of mother to child transmission. Therefore, factors contributing to viral suppression should be enhanced as much as possible in pregnant women as lack of that:

(i) Fails to achieve elimination of mother to child transmission

(ii) Adds more cost to the country with more expensive drugs for second line regimes which can lead to even poorer adherence due to pill burden

(iii) Which further poses difficulty in choice of ART regimens for children who may be infected from women who might find themselves on the second line regimen

There is therefore a literature gap in this area in Lesotho. This study will help strengthen Lesotho's health system in terms of HIV infected pregnant and breastfeeding women and their ART adherence. The aforesaid will assist in improving retention and viral load suppression, which will eventually lead to the elimination of mother to child transmission.

1.4 Literature Review

A: FACTORS AFFECTING VIRAL LOAD SUPPRESSION

1.4.1 Adequate Adherence Relating to Proportion of Pregnant and Breast-Feeding Women with Viral Load Suppression

Studies prior to 2005 where older ART regimens were used implied that continual viral load suppression is attained only if more than 95% of doses prescribed are acquired (37). However, studies with newer drugs like NNRTIs e.g. efavirenz or ritonavir-boosted protease inhibitors (PIs) regimens, indicate that virological suppression is achievable with moderate levels of 70% to 80% of adherence in ART (38). This is due to higher effectiveness and prolonged half-lives of the newer ART regimens which are more lenient of irregular doses missed (38). Nevertheless, in Lesotho adequate adherence still ranges between 95-105% as optimal measure regardless of the type of regimen.

Cross sectional studies led in rural Nigeria and South Africa urban backgrounds demonstrated that knowledge of women to ART enhanced suppression (39) (40). One study observed that women not adherent to their ART were unlikely to attain viral suppression in comparison to their counterparts who were (41). Despite non-adherence escalating the risk of virological non-suppression, HIV disease prognosis and possible attainment of drug resistant virus, poses an increased risk of mother to child transmission (34). It is apparent that consistent adherence on ART is key in viral load suppression. A systematic review and meta-analysis made by 51 countries confirmed 73.5% overall ART adherence with pregnant women better than those in postnatal period (42). This was also consistent with what was reported in Malawi with a lower adherence at 66% in 3 months postpartum period and higher adherence at 73% during pregnancy (43). In the evaluation of adherence in low, middle- and high-income countries, the collective proportion of satisfactory adherence was evidently higher in the antepartum period at (75.7%, 95% CI 71.5–79.7%) than during postpartum (53.0%, 95% CI 32.8% to 72.7%) (p value=0.005) (33). Since adherence has been established to be important for viral load suppression, when it is evaluated for both pregnant and breastfeeding women, from the studies it is evident that, during breastfeeding period women turn to struggle more with adherence issues than in pregnancy. In general, virological non-suppression seemed to be higher amongst patients with reported

adherence below 85% (44) in a systematic review in Sub-Saharan Africa. A study in Northern Uganda also stated that having missed an appointment in the past 6 months made women twice likely not to take their medication adequately (45). Therefore, it is imperative to not only evaluate adherence calculations without exploring the patterns patients on ART have with regard to missing appointments.

1.4.2 Clinical Factors Affecting Viral Load Suppression

Among suspected treatment failures, breast feeding seemed to increase the odds of viral non-suppressed when subgroups in Uganda were analysed (46). This is due to increased psychosocial-stressors during this period and lack of counselling on being virologically suppressed (18) as stated in the UNICEF report. A study in Uganda showed high rates of viral suppression apparent throughout periconception at 97%, during pregnancy at 93% and at postpartum at 89% (47). Kenya with a suppression rate at 78.9% (48). These findings suggested that women may need more support during this period of breastfeeding. It is evident from the studies that breastfeeding period is a risk factor for women on ART to be unsuppressed.

Another study in South Africa established that women who commenced ART at their current pregnancy and achieved viral load of ≤50 copies/mL during delivery, in their subsequent monitoring by 12 months in their postpartum period almost 30% were unsuppressed with a viral load greater than 1000 copies/mL (49). This further reiterates the increased risk of being unsuppressed viremia during breastfeeding period and therefore an increased risk of transmission. Many reasons which can pose difficulties during the postpartum period have been suggested in studies. Personal obstacles to adherence to treatment include postpartum depression, as well as pill burden or drug regimen frequency (33). Post-delivery also has its own challenges which include physical, emotional and economic stresses, added to these is the burden of caring for a new baby, which likely contributes to poor adherence (33).

Significant protective factors were found, for Brazilian women who received their HIV positive results during their antenatal period in terms of MTCT (RR 0.16, 95% CI 0.05–0.53) and initiated ARV treatment in the same period (RR 0.14, 95% CI 0.08–0.25) (50). Women who commenced ART whilst breast-feeding were also two times more likely not to adhere to their follow-up visits. This was compared to pregnant women who were initiated on ART (42). Other studies suggested that the improved adherence when women are pregnant than during

breastfeeding may be due to maternal concerns to prevent MTCT to the foetus during the antepartum period (33). However, regardless of pregnancy being suggested to be a protective factor in being virally suppressed, different studies also had a different view in this regard. Since "Morning sickness" happens a lot during the early days of pregnancy, this may contribute to the decrease in adherence during pregnancy (51). Of women who are pregnant, 70-85% of them are subject to nausea and vomiting, a situation which can be aggravated by other ARVs, making it difficult to adhere (33). As much as pregnancy has been stated as more protective towards adherence to ART and viral load suppression than during breastfeeding period, the timing of commencing ART during the pregnancy period is vital. During the earlier trimester when morning sicknesses are quite prominent then may bring challenges in taking the medication.

In another study, patients with WHO stage 4 seemed to have a higher viral non-suppression rate (45). It was therefore suggested that being classified as WHO stage 1, 2 and 3 can be linked with the likelihood of being virally suppressed. Patients with active tuberculosis (TB) are prone to being virologically unsuppressed (46). Aside from the physiological reasons known to how active TB contributes to high viral load; pill burden was regarded as a risk to not being suppressed by one of the nurses in Uganda (45). Health factors such as the advanced AIDS stage were also said to be the cause of non-adherence during pregnancy (33). This might possibly be due to the increased burden of pills as the advanced AIDS stage comes with other opportunistic infections. In Malawi, 19 facilities demonstrated that initiating ART amongst women who are pregnant with a high CD4 cell count were five times more likely to not adhere in follow-up visits (42), compared to those with a lower CD4 count.

Other clinical factors included previous exposure to ART, being introduced to ART later in gestation, past history of tuberculosis and first-time pregnancy were associated with a high VL during the delivery period (52). Women who were transferred from other clinics were also said to have challenges with viral load suppression as well (53). This could suggest that there could already have been some challenges in the parental site with adherence.

1.4.3 Socio-Demographic Factors Affecting Viral Load Suppression

Different age groups in the HIV infected adult population is considered a risk factor for viral non-suppression as it decreases with increasing age (46). This was further reiterated in the study in Northern Uganda where health care providers stated that lack of viral suppression was mainly

in late adolescence (45). Younger age was also associated with cessation of ARVs (54) therefore causing virological failure. Moreover, younger age 18-22 years was independently associated with viremia episodes after initial viral load suppression compared to those greater than 34 years of age (49). Overall, younger age has more challenges with adherence to ART and therefore difficulty with viral load suppression. With challenges already discussed in pregnancy and breastfeeding women, it is possible that young women face even greater challenges of viral load suppression with an additional added stress of pregnancy and breastfeeding to the continuity of care in ART.

A significant aspect related to a higher adherence to ART from other studies was the disclosure of one's HIV status for social support, which was in accordance with other studies about the general population (55). Disclosure has been demonstrated to be protective for viral suppression as an enhancer of adherence (56). There has been a couple of studies that have found an association between virological failure and nondisclosure (57). Despite the enduring HIV/AIDS epidemic, stigma still prevails in the current decade which may compromise continuity of care after pregnancy (54) as it is common that there are supplements which pregnant women take and can easily be masked for ART during pregnancy but not beyond it if disclosure has not been made.

The lack of confidentiality was cited as one of the factors which may hinder uptake of PMTCT services. This is because women assume that people will link their HIV positive status when she stops breastfeeding his/her child earlier than the cultural norm (58) which further indicates stigma and lack of disclosure as a common problem to non adherence. Belief systems of individuals played a critical role as well to their adherence. Some women specified that their pastors had informed them to stop taking ART as they were healed whilst some who also use traditional medicines were informed not to use ART simultaneously with ART (59).

The postpartum period includes various changes such as psychological, social and economic changes that may affect a mother's health-related behaviours (60). This period may further include geographic mobility and having a better understanding on how this phenomenon may influence adherence and care (27) is important for better support. Therefore, the distance from where patients reside to where they access health services may cause disengagement from care for those who cannot afford transport (27). Access of health services into the communities is

also important as distance to health facilities may be a hindrance to women adhering to their ART refills dates and maintaining a suppressed viral load.

Additionally, some women during the postpartum period stop adhering to their ARV medications to avoid disclosure that comes along following delivery since they can no longer mask ARVs as prescribed prenatal medication (61). It was mentioned that despite the spouse being supportive, relatives can be the one who end up discriminating against a woman and therefore can cause them to be fearful to continue with ART (58). Furthermore, it has been recognisable that women who are initiated on ARV without any symptoms have difficulty with engaging in either PMTC services or adhering to ARV (61).

Lack of male partner has also been noted to be a barrier in PMTC in the pregnancy period (54). In a study done in Malawi, it was established that spouse's do play a significant role in the decisions made to whether a woman accesses PMTCT services or not as they fear divorce (62). However, from the study it was evident how negatively it can affect uptake, especially when most men had limited knowledge towards PMTCT services (62). In African settings, women continue to be marginalized in decision makings due to cultural practices which disproportionately affect access to quality health care services (63).

1.4.4 Drug Factors Affecting Viral Load Suppression

The biological plausible explanation of poor adherence is the result of drug dosages below the levels necessitating production of therapeutic effect and therefore enabling existence of drug resistance (64). The Kabeho study in Rwanda demonstrated an increasing proportion of women with detectable viral suppression on ART for more than 36 months (65). This was attested by one study stating that ART duration greater than 3 years also increased the risk of viremia marginally (66). This may suggest that a longer duration of being on ART is a risk factor probably due to treatment fatigue. A study done in Kwazulu-Natal South-Africa, non-TDF regimens had a significant increase to high viral load by sevenfold (66). This may have been due to lack of combined ART pills in those regimens as adherence was better in a combined regimen (33). Therefore, it is important to note that being on a Tenofovir based regimen has been suggested to improve viral load suppression as it comes as a combined drug which is easier to administer.

Side effects were cited as a cause for suspending ARV medications in previous studies, despite the current regimen with fewer side effects in comparison to the phased out old regimen (61). Women indicated in one study, that they are more distressed by the side effects as they can evidently indicate their HIV positive status (67). There has been documentation that the previous intermittent short-course ART regimens that were used in prior pregnancies of HIV positive women who were not eligible for life long ART, resulted in archived drug resistance (68). Establishing the previous ARV drug history is important as exposure to any of the drug can archive resistance and despite adequate adherence, the woman fails to suppress it.

1.4.5 Health System Challenges Affecting Viral Load Suppression

Sources of non-adherence vary. One example is the fragmented health systems, requiring women to attend different clinics or be transferred soon after delivering a baby (18). A major hindrance to the uptake of PMTCT ARV is shortage of trained nurses (35). This was further emphasized in a study in Malawi where lack of trained nurses for counselling and testing led to limited counselling (58). This leads to high patient volume, long queues and waiting-times, brief or poor quality of sessions for counselling and record keeping (18). Adequate counselling provided to women influence uptake of PMTCT services including adherence to ARVs (61). These health services' barriers negatively affect timely testing, the swift return of test results, and urgent intervention to an elevated VL (35). Patients who have also had an encounter of negative staff attitudes were cited as one of the reasons for not returning to facilities (35). Negative treatment during service delivery by staff at the clinic was mentioned to be one of the factors that can contribute to non-adherence (54). In one study where women who had disengaged in care during their pregnancy or breastfeeding period were followed, one stated that she never returned to the clinic after the provider yelled her name stringently along the courtyard after completing with her so that whoever is within ears length should know about her status (67). Lack of confidentiality and a discriminating attitude of clinicians can cause drop out in care and without drugs women can't be suppressed.

Interventions implemented in ending paediatric AIDS by eliminating mother to child transmission are complex programmatically, as they involve various levels in the health system (13). Accordingly, for optimum outcomes, evidence-based interventions need implementation within robust health systems at community level and facility levels (13). After delivery, many

women encounter a reduction in their contact with the health system and remain unaware that they should continue and remain on treatment during breastfeeding period (24) and cause less encounter with the health facilities where health education is provided for continuity care and infant's HIV free survival even during breastfeeding period discussed. This reduces prospects of emphasizing on the adherence messages (24). Several studies have indicated that visits in care worsen during the breastfeeding period (27). This might be attributed to priority being more focused on infants than their mothers postnatally. The domains of maternal and child health globally, pay more attention to mothers prenatally in providing effective antenatal care, with the aim of safe delivery to promote child survival (69) which swiftly change after delivery to being on the infant. Some of the contributing factors might be due to insufficient exploration of differentiating care for ART services models amongst pregnant and breastfeeding women yet these models have generated substantial interest (27) for the general adult population in care. Women in Tanzania who fell out of PMTCT care indicated concerns around frequent facilities attendance which clashes with competing economic priorities and lack of privacy within the facilities (67). Suboptimal adherence has also been reported in patients that needed to travel long distances to access health-care (70) and therefore affecting their viral load suppression. One study in Malawi suggested factors which are associated with lack of retention of women in care as receiving ART care at high volume facilities (71) and therefore poor adherence to lifelong treatment.

1.4.6 Conceptual framework

A framework is the general concept which underpins a study. When the basis of a study is on a specific theory, it is referred to as the theoretical framework whereas one that is based on the specific concept is a conceptual model even though often interchangeably used (72).

The study analysis assumed ART adherence as an independent factor for viral load outcome in the conceptual framework. Other confounders included; socio-demographic factors (age, disclosure, stigma, marital status and belief systems), clinical factors (breastfeeding period, diagnosis of HIV prior to pregnancy, WHO stage and parity, biological factors (high baseline viral load, baseline CD4 count), drug factors (duration of ART, number of pills/pill burden, side effects, previous exposure to ART) and health system factors (confidentiality, access to health

services, trained nurses in a facility, quality of adherence sessions and differentiated service delivery models).

Socio-demographic factors are a proximal role towards adherence as they consist of social and partner relationships, age, disclosure of HIV status and social support (73). Physiological and biomedical considerations are included under clinical and drug factors as there are physiological changes that occur during pregnancy and breastfeeding period, HIV status and ART related concerns that can hinder adherence (74) and eventually viral load suppression. The figure below summarises how these factors relate to each other;

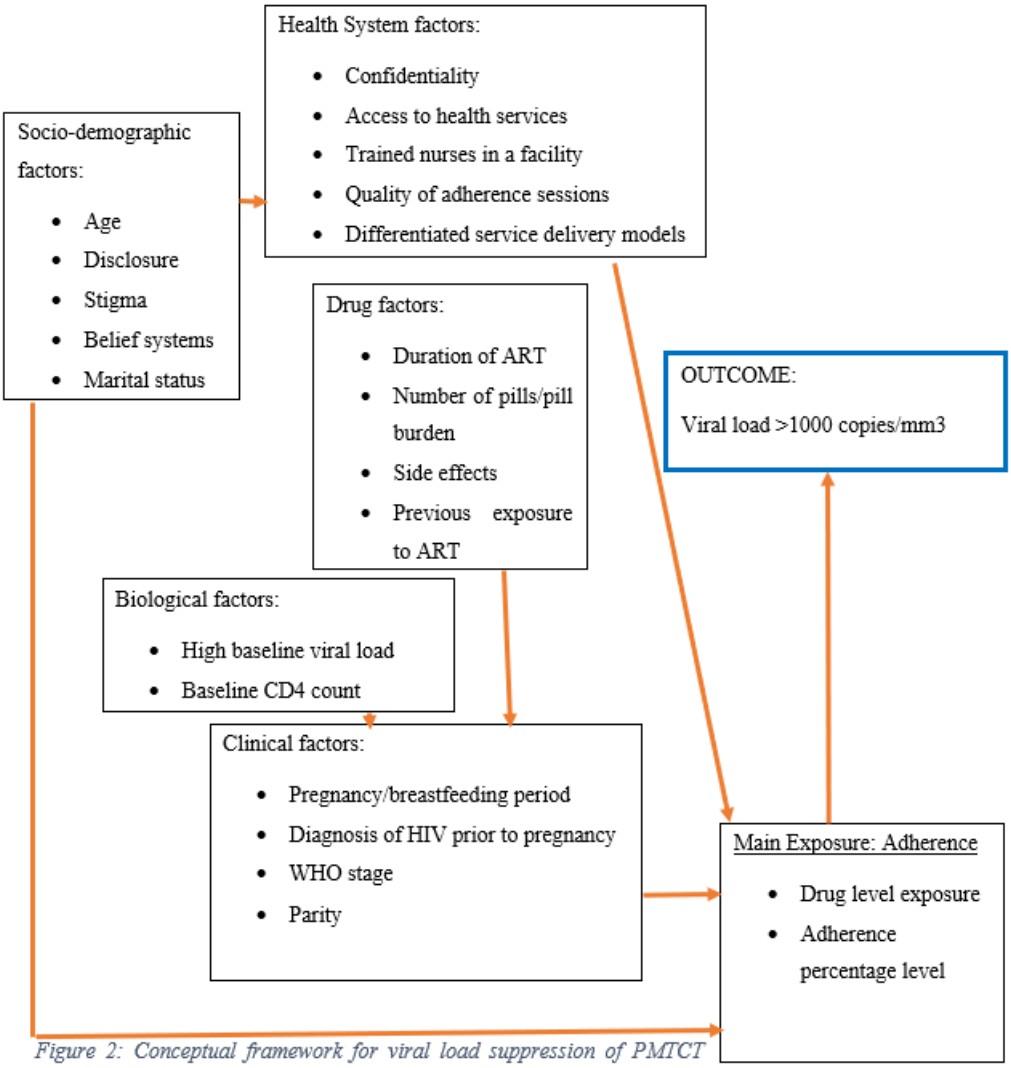


Figure 2: Conceptual framework for viral load suppression of PMTCT women

As shown in the above figure, there is a direct link of adherence to viral load outcome results. Socio-demographic, biological, clinical, health care system and drug factors have a direct link to adherence in terms of drug level exposure and inevitably causing treatment failure.

B: THE ASSOCIATION BETWEEN MATERNAL VIRAL LOAD SUPPRESSION AND INFANT DNA PCR POSITIVITY

1.4.7 Elimination of Mother to Child Transmission and DNA-PCR

Global targets related to MTCT had been included in the Millennium Development Goals (MDGs) 2000–2015 and Sustainable Development Goals (SDGs) 2015–2030 (75). Global coverage in providing services that support prevention of mother-to-child transmission of HIV amplified tremendously, from 50% [44-56%] to 77% [69-86%] in 2010 and 2015 respectively (24). This has then resulted in a decline of 51% in new HIV infections amongst children 0–14 years since 2010 (24). Evidence that emerged showed that timely initiation of antiretroviral (ARV) drugs substantially decreased mother to child HIV transmission with triple ART being the key to eliminating transmission (13). PMTCT recommendations have transitioned and simplified from single-dose nevirapine (NVP) to lifelong ART for every HIV-positive pregnant and lactating woman despite the status of their immune system (13).

Without any treatment, 35– 40% of infants born from HIV-infected mothers can be infected perinatally, during delivery, or even the period of breast-feeding (8). Interventions meant to lessen MTCT have focused on the intervals of exposure and have included ART initiations, caesarean section prior to onset of signs of labour or membranes ruptured, and total breastfeeding avoidance (76). When these interventions are combined and followed efficiently, countries can decrease MTCT risk to as minimal as 1-2% (77). Countries like Botswana, provide PMTCT ART services for free and vertical HIV transmission can be reduced from 35% to 5% (78) when women are virally suppressed. UNAIDS 2016, stated that Lesotho has achieved a decline of between 20%-49% in new HIV infections amongst children of 0-14 years as amongst low and middle-income countries between 2010-2015 (24). According to global guidance, countries are considered to have eliminated mother to child transmission when they have attained and sustained for a minimum of a year:

(i) New paediatric HIV infections of ≤50 per 100 000 live births due to MTCT (79)

(ii) HIV MTCT rate of <5% for lactating countries and for non-lactating countries at <2% (79).

EID testing to rule out HIV infection for exposed children who are breastfed is done:

(i) In the first 3 months of life (79),
(ii) Followed-up by serological testing (e.g. at 9 months) (79)
(iii) With a final antibody testing at 18 months or 3 months after the cessation of breastfeeding to rule (79).

WHO, has recommended in 2014 that countries should attain greater than 95% of ANC and HIV testing coverage amongst all eligible pregnant women) and greater than 90% of ART coverage amongst those who are HIV-positive (13).

There was also correlation established between maternal ART adherence rates to Mother To Child rates (Pearson correlation r = −0·072, p= 0·751) (33) and transmission directly relative to maternal viral load (52). Vertical HIV infection persists to occur and the utmost burden of incidence in Sub-Saharan Africa (52) accounting for almost 14% of all global new HIV infections (80). Neighbouring countries have managed to achieve the Global Plan milestone mainly, South Africa at 2%, Uganda at 2.9%, Swaziland at 3.3% and Namibia at 4.1% (81) at the end of breastfeeding period while Lesotho is at 9% in 2020 (25) whilst using UNAIDS estimates. DHIS 2014 stated an increase from 6.93% at 6 weeks to 12.4% after breastfeeding indicating challenges which may still persist during lactation period. A substantial number of infants are stated to be infected during breastfeeding period (24). Currently, Lesotho is still doing DNA PCR during 6 and 14 weeks for HIV exposed children (7).

Vertical transmission risk was 0.25%, 2.0% and 8.5% amongst women with VL less than 50, between 50 to 1000 and greater than1000 copies/mL at delivery, respectively (52). Another study indicated that with high viral load levels greater than 1000 copies/ml, vertical transmission rates have been reported to even be at 30% (82).

1.4.7 Conclusion

Virological monitoring is the best way of determining treatment failure. The rates of virological failure in pregnant and breastfeeding women differ from country to country. Factors that are associated with virological failure in pregnant and breastfeeding women include adherence,

WHO clinical stage, timing of ART initiation in the ANC period, support system, ART regimen and attitudes or service delivery within health facilities. These factors can be used as a prognostic tool in identifying pregnant and breastfeeding women at high risk of treatment failure. Factors affecting viral load suppression specifically for pregnant and breastfeeding women have not been explored in Lesotho as there is a literature gap in that area. The study will therefore further help in strengthening the health system relating to HIV infected pregnant and breastfeeding women on their ART adherence. The aforesaid will assist in improving retention and viral load suppression amongst them and therefore reduce mother to child transmission.

This study seeks to describe factors contributing to viral load suppression amongst HIV infected pregnant and breast-feeding women and association of maternal viral load suppression to infant DNA PCR positivity.

1.5 Objectives

1.5.1 Main Objective

PRIMARY OBJECTIVE:

To describe factors contributing to the suppression of viral load amongst HIV infected pregnant and breast-feeding women who have completed 6 months of ART treatment.

SECONDARY OBJECTIVE:

To associate maternal viral load suppression to infant DNA PCR positivity in Maseru, Lesotho.

1.5.2 Specific Objectives

- To determine the proportion of suppression of viral load amongst pregnant and breast-feeding women.
- To describe factors affecting the suppression of viral load amongst pregnant and breast-feeding women.
- To establish the association between viral load suppression and the infant DNA PCR positivity rate amongst breast-feeding women.

Chapter 2: Methodology

2.1 Introduction

This chapter describes, methodology used to conduct the research study on factors contributing to viral load suppression amongst pregnant and breastfeeding in Lesotho. The research study design, study population and sample, data collection method, data analysis and ethical considerations will be discussed.

An overview of the Kingdom of Lesotho is that it is a small, mountainous country which is landlocked in Southern Africa and entirely surrounded by the Republic of South Africa (83). The country has 10 districts with a total area of about 30,355 square kilometres and divided into four ecological regions as: Lowlands, Mountains, Foothills, and Senqu River Valley (23). The country has a mountainous terrain which poses challenges with accessibility to services for its wider population (23). The population of Lesotho was estimated to be 2,173,390 in 2017 with the 72% of the Basotho in rural areas (84).

The health delivery system is structured as 372 health facilities in Lesotho comprising of 2 specialised hospitals, 1 referral hospital, 18 district hospitals, 188 health centres, 3 filter clinics and 48 private surgeries, 66 nurse clinics and 46 pharmacies (83). The Ministry of Health owns 42% and 58% health centres and hospitals respectively whilst Christian Health Association of Lesotho CHAL owns 38% and 38% of health centres and hospitals respectively (83).

2.3 Study design

This is a descriptive, cross-sectional study on HIV positive pregnant and breastfeeding women using secondary data analysis from the Lesotho District Health Information system (DHIS) to identify patients' files and cards in order to retrieve detailed records.

2.3 Study setting

The study was conducted in Maseru district, Lesotho. Maseru is the second highest HIV prevalent district with 27.3% after Mohale's Hoek with 29.3% (5). It is amongst the four districts with the greatest populations with others as Leribe, Mafeteng and Berea, comprising 62.2% of the country's population (6). Maseru also has the highest density urban areas which carry more HIV burden than in the rural areas with HIV prevalence of 27% and 21% respectively (6). It has 3 sub-districts named after the district hospitals: Queen II hospital, Scott hospital and

St Joseph's hospital. The district has 42 facilities which are mixed as rural, peri-urban and urban settings. Initially, an assessment of the extent of viral suppression will be conducted in all of these facilities. Facilities found to have pregnant or breastfeeding women who are unsuppressed were the key facilities for further study for purposes of this research.

2.4 Study Population

Study population included all HIV positive pregnant and breastfeeding women on ART in the Maseru district. Female population is 51.1% of the entire national population with 26% of females of reproductive age (85).

2.5 Sample size calculation

Consolidated available data in Sub-Saharan Africa shows viral suppression rates during delivery or immediately postpartum range from 30% to 98% (86) whereas for pregnant women at 79% to 91% of viral load suppression of less than 1000 copies/ml (52). Therefore, the sample size was determined using StatCalc by taking prevalence of viral load suppression amongst pregnant and breastfeeding women for the previous studies.

The minimal sample size was then calculated for both groups pregnant and breastfeeding women using a marginal error of 5% at 95% confidence interval. Therefore,

$n=\frac{z_{\frac{\alpha}{2}}^2 pq}{m^2}$ for pregnant women	$n=\frac{z_{\frac{\alpha}{2}}^2 pq}{m^2}$ for breastfeeding women
$=1.96^2$x0.79x0.21 $/0.05^2$ (79%) =	1.96^2x0.3x0.7$/0.05^2$(30%)
$=1.96^2$x0.91x0.09 $/0.05^2$ (91%) =	1.96^2x0.98x0.02$/0.05^2$(98%)
=255 cases for infinite population=	323 cases for infinite population using
using 79% prevalence	30% prevalence
=126 cases for infinite population=	30 cases for infinite population using 98%
using 91% prevalence	prevalence

However, since a finite population is already known at 9 cases for pregnant women and 115 cases breast feeding women calculations can be based on that using a formula:

$n=\frac{n_0 N}{n_0+N-1}=$	$\frac{n_0 N}{n_0+N-1}$

$= \frac{255 \times 19}{255+18} = \frac{323 \times 121}{323+120}$

=18 case for 79% prevalence = 88 case for 30% prevalence

$= \frac{126 \times 19}{126+18} = \frac{30 \times 121}{30+120}$

=17 case for 91% prevalence =24 cases for 98% prevalence

The calculated sample sizes for pregnant and breastfeeding women with viral load >1000copies/mL is 106 (18 cases for pregnant and 88 cases for breastfeeding). However, given the small number of unsuppressed women (140 for the entire Maseru district) and in order to improve the power of the study all 140 participants with viral load >1000 copies/mL were included in the study instead of 106 suggested by the sample size calculation. The ratio of 1:2 for unsuppressed to suppressed participants was also used to increase the power of the study and to avoid empty cells when comparing viral load suppression by socio-demographic and clinical variables. Unfortunately, as it will be seen in chapter three, the sample size did not achieve the objective of avoiding empty cells 100 percent.

2.5 Study sample selection

Systematic random sampling was used to select participants with viral load of <1000 copies/mL at each facility maintaining the ratio of 1:2 for unsuppressed and suppressed participants. In this study viral load suppression was defined according to the Lesotho ART policy as <1000 copies/mL (17). Figure 1 presents the process used to identify the study participants;

Figure 1: Sample selection and size

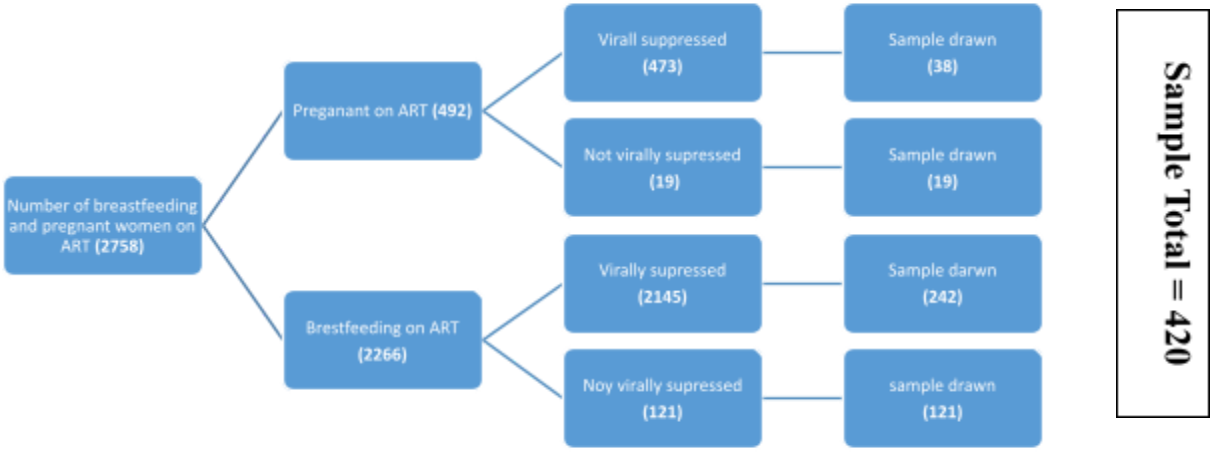


Figure 3: Sample selection and size

All pregnant and breastfeeding mothers on ART for more than 6 months but not virally suppressed were included in this study. In order to increase the power and compare between those suppressed and not suppressed, a comparative group for those suppressed was also systematically selected from the same facility. For every virally unsuppressed pregnant/breastfeeding woman, two suppressed cases were randomly selected through stratified random sampling using the process below:

- Firstly, the sampling interval was calculated by dividing the total number of participants in each population from the filing system as pregnant or breastfeeding women who are placed by order of their unique numbers by the number needed for the sample
- E.g. If there are two unsuppressed women, to find 4 cases suppressed out of 40 in their filling cabinet will mean 40/4. Therefore, the 10^{th} intervals were used to make selection
- The first card in the comparative suppressed participants was always the starting point
- Counting was then started with the first ART card and counting down the list selecting each n^{th} participant interval.
- When the end of the list was achieved, the desired number of comparative participants was achieved

- As shown in the above figure, a total of 420 women on ART were included of whom 140 were not suppressed and 280 were virally suppressed.

2.5.1 Inclusion Criteria

All pregnant and breastfeeding HIV positive women on ART for at least 6 months in Maseru health facilities were eligible to be included into the study.

2.5.2 Exclusion Criteria

All those on ART but neither pregnant nor breastfeeding were excluded participants. In addition, those who were on ART for less than 6 months and those who had no viral load results or adherence calculations in their ART cards were also excluded.

2.6 Data collection

Data was collected in the month of July 2020 by the researcher from the 20 sites out of 45 sites identified through DHIS which had qualifying participants. Socio-demographic and clinical characteristics were then extracted from these ART cards. She had undergone an ethical training for introduction to research ethics.

2.6.1 Data collection tool

Two data extraction excel sheets were developed and used to extract data (Appendix 2). Patient level data were collected from patients' individual files after utilizing MOH database system for facilities with pregnant and breastfeeding qualifying women to participate in the study. The data collection tools provide details of the data collected.

2.6.2 Data collection process

Data collection started with review of electronic data from DHIS where 20 out of 45 facilities with breastfeeding and pregnant women qualifying to be included in the study were identified. The researcher went to all the 20 facilities and retrieved files and cards for these cases. In addition, files and cards from the selected pregnant and breastfeeding women were also systematically retrieved as described above. Using the above data collection tool, manual review of records was done, and data retrieved into the data collection tool.

2.8 Variables

The dependent variables (outcome of interest) were first virological failure and DNA PCR results of the child. Virological failure was defined as a plasma viral load of >1000copies/ ml

blood. The DNA PCR result of the child was either positive or negative. While virological failure was for the whole study sample, DNA PCR was explored for breastfeeding women who were virological unsuppressed.

Independent variables included both demographic and clinical characteristics. Demographic variables of the study included the age (Number of completed years), marital status (married, single or previously married), Partner's HIV status (positive, negative or unknown), terrain of facility accessing ART (rural, peri-urban and urban) and the type of facility in terms of whether run by Government, Christian Association of Lesotho (CHAL), Private or Private-Government.

Independent clinical variables included: duration of ART, dosage of regimen when viral load was taken, total number of drugs taken a day, average adherence in the last 6 months, type of regimen, WHO stage at ART initiation, ever defaulted from ART treatment, knowledge of HIV status before or during pregnancy, completion of 3 adherence sessions and number of staffs in MCH ART corner.

2.9 Data Analysis

Data from the record reviewed was entered into an Excel spreadsheet for cleaning before being exported in SPSS for analysis. The prevalence of an unsuppressed viral load (>1000 copies/ml) was calculated as a proportion of those with a viral load result after at least 6 months of treatment with viral load results. At bivariate analysis level chi square statistics was used to assess existence of associations between different exposures and virological suppression. Regimen use by less than 5 participants were excluded from the analysis. A p-value of < 0.05 was deemed statistically significant in this analysis. Multivariate analysis by way of a stepwise conditional logistic regression model was performed with virological suppression as the response variable. However, there were variables which could not be entered into the regression mode due to empty cells. These are variables with 100% unsuppressed viral load due to no suppressed participants for the variable. The variables in question include adherence, has ever defaulted from treatment, total drugs taken and drug dosage. The criteria used for selecting variables possible for including in multivariable analysis were on the basis of p-value of less than 5% and all variables that were significantly associated with virological suppression were entered into the model to identify factors independently associated with virological suppression. Factors associated with DNA PCR positivity among breastfeeding women with viral load >1000 copies/mL was also explored.

Recent DNA PCR results for individual infants were utilized either as 6 weeks or 14 weeks. Variables that were found to be statistically associated with the two outcome variables (virological suppression and DNA PCR positivity) at bivariate analysis level were all entered into the logistic regression model. Variables associated statistically with the two outcome variables (virological suppression and DNA PCR positivity) at bivariate analysis level were all entered into the logistic regression model. The data was also be saved into cloud. Table 1 presents a summary of all study variables and the suggested statistical analysis plan.

Table 1: Variables and Statistical analysis plan.

Variables	Statistical analysis Plan
Objective 1: To determine the proportion of suppression of viral load amongst pregnant and breast-feeding women. ● continuous variables of viral load results of pregnant and breastfeeding women on ART ● then categorical of viral load >1000 copies or <1000 copies	● frequency ● proportion ● tables or charts used
Objective 2: To describe factors affecting the suppression of viral load amongst pregnant and breast-feeding women SOCIO-DEMOGRAPHIC ● age (continuous) ● marital status(categorical) ● Clinic terrain (categorical) (rural, peri urban or urban) ● Type of clinic (CHAL, government or private) (categorical) ● WHO clinical staging(categorical) ● any missed appointment in the 6 months(categorical) DRUG FACTORS ● duration of ART since initiation (continuous)	● Descriptive statistics of Mean and standard deviation will be used for normal range and skewed ranges will be in median and interquartile range ● Continuous variables were tested for the assumption of normality using histograms, normal quantile plots and standardised normal probability plots however medians and interquartile ranges were used to summarize all the continuous variables as none of them were normally distributed.

<table>
<tr>
<td>

average adherence in the past 6 months (continuous)
Type of regimen (continuous)
Frequency of taking ART regimen (continuous)

HEALTH SERVICES

completion of 3 adherence sessions given (categorical)
CLINICAL FACTORS

knowledge of status before pregnancy or after (categorical)
pregnancy or breastfeeding (categorical)
WHO Staging (continuous)

</td>
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For categorical variables, Chi-test was used
odds ratio and confidence interval or p value of <0.05 would be considered statistically significant

</td>
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<td>
Objective 3: To establish the association between viral load suppression and the infant DNA PCR positivity rate amongst breast-feeding women.
A table of exposure and outcome done
<table>
<tr><td></td><td>DNA pcr +</td><td>DNA pcr -</td></tr>
<tr><td>VL>1000</td><td></td><td></td></tr>
<tr><td>VL<1000</td><td></td><td></td></tr>
</table>
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<td>

Odds ratio and 95% confidence interval
Conditional logistic regression model will be used as well between viral load >1000 copies/mL to DNA PCR positivity

</td>
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</table>

2.10 Ethical consideration

Ethical approval was obtained from the ethics committee of the University of Witwatersrand. The Research Ethics Committee of the Ministry of Health Lesotho also granted ethical approval with waiver of informed consent for using medical records. The researcher also did the introductions to Ethics training under the Training and Resources in Research Ethics Evaluation courses to understand confidentiality and breach of confidentiality. Approval permitting for the rights to use DHIS II for part of the routine data to identify sites was also granted. Permission to review records of pregnant and breastfeeding women on ART for the identified period was requested from the nurses in charge of the clinics. None of the names or unique numbers of the

clients on ART were used in order to maintain confidentiality and case numbers were provided for each participant.

Chapter Three: Results

3.1 Introduction

This chapter gives a presentation of the results of the study with the aim of addressing the objectives of the research. A description of socio-demographic and clinical characteristics of the study population will open the chapter. The viral load suppression prevalence for different socio-demographic and clinical variables presented. For each variable the relationship between viral load suppression and the variables was explored through the use of Chi-Square statistic. The associations between suppressed viral load and socio-demographic and clinical characteristics were determined through the use of logistic regression. The association between DNA PCR and socio-demographic and clinical variables was explored through the use of Chi-Square statistics among women with viral load >1000 copies/mL. The chapter closes with an identification and report of the characteristics that were associated with viral load suppression net of other variables through the use of multivariable analysis.

3.2 Profile of Study Population

Reference to Figure 2: Sample selection and size, a total of 2758 pregnant and breastfeeding women were on ART in the Maseru district. To establish the first objective of the study that was to determine the proportion of suppression of viral load amongst pregnant and breast-feeding women. Two thousand two hundred and sixty-six (94.7%) of those breastfeeding and 492 (96.1%) of those pregnant were virally suppressed.

3.2.2 Proportion of viral load suppression

To determine the proportion of viral load suppression, health centre records were used. Proportion of viral load was calculated separately for pregnant and breastfeeding women. The proportion was further categorized by type of facility i.e. CHAL, GOV, private or private-GOV and terrain to establish any differences. Proportions of viral load suppression are presented in Table 2.

Table 2: Viral load suppression by facility and terrain (%)

Type of facility / Terrain	Category	Suppressed Breastfeeding women	Breastfeeding women not suppressed	pregnant women suppressed	pregnant women not suppressed
Type of Facility	**CHAL**	563 (94.9)	30 (5.1)	167 (98.2)	3 (1.8)
	GOV	1224 (93.5)	85 (6.5)	227 (93.8)	15 (6.2)
	MCC	173 (100)	0 (0)	27 (100)	0 (0)
	Private	7 (100)	0 (0)	21 (95.5)	1 (4.5)
	Private-GOV	178 (96.7)	6 (3.3)	31 (100)	0 (0)
Terrain	**Peri-Urban**	261 (96.7)	9 (3.3)	118 (96.7)	4 (3.3)
	Rural	500 (93.8)	33 (6.2)	64 (91.4)	6 (8.6)
	Urban	1384 (94.6)	79 (5.4)	289 (97.0)	9 (3)
Total		2145 (94.7)	121 (5.3)	473 (96.1)	19 (3.9)

Majority of breastfeeding women were from government facilities at 1309 (58%) and urban facilities at 1463 (65%). Suppression rate for breastfeeding women was at 94.7%. Suppression rates by CHAL, government, MCC, private and private-government was at 94.9%, 93.5%, 100%, 100% and 96.7% respectively for breastfeeding women. For terrain, suppression rates were respectively 96.7%, 93.8% and 94.6% for peri-urban, rural and urban facilities for breastfeeding women.

Similarly, 242 (49%) of pregnant women were getting services from government hospitals as the majority and followed by CHAL facilities at 172 (35%). Two hundred and ninety-eight (61%) of pregnant women were getting services from health facilities located in urban areas, 122 (25%) in peri-urban and 70 (14%) in rural settings. In terms of suppression rates amongst pregnant women, 95.7%, 93.6%, 100%, 96.6% and 97.2% were suppressed respectively for CHAL, government, MCC, Private and private-government respectively. Corresponding suppression rate figures for terrain were 96.7%, 93.5% and 95% for peri-urban, rural and urban respectively.

3.2.3 Socio-Demographic Profile

Assessment of the socio-demographic characteristics of the study participants was done to determine categories such as age, marital status, partners HIV status, terrain of facility accessing

ART and the type of facility for a deeper understanding of the participants description. See table 3.

Table 3: Socio-demographic characteristics

Variable	category	Percent	N
Status	Breastfeeding	86.4	363
	Pregnant	13.6	57
Marital status	Single	11.9	50
	Married	86.7	364
	Previously married	1.4	6
Age	<25	11.9	50
	25-29	48.3	203
	30-34	24.5	103
	35-39	11.4	48
	40+	3.8	16
Mean		29.21	
Mode		28	
Median		28	
Range		17-49	
Partners HIV status	Negative	14.0	59
	Positive	64.8	272
	Unknown	21.2	89
Terrain of facility	Rural	27.1	114
	Peri-Urban	8.6	36
	Urban	64.3	270
Type of facility	CHAL	27.1	114
	GOV	66.4	279
	Private	0.7	3
	Private-Gov	5.7	24
	Total	100.0	420

The majority (86.4%) of participants were breastfeeding women whilst pregnant women formed 13.6% of the participants. Eighty seven percent (86.7%) of the participants were married women and 11.9% were single. With regards to age, 48.3% of the participants were aged between 25-29 and 24.5% of the participants were aged between 30-34. The mean age was 29.21 years with a standard deviation of 5.2 years.

More than three quarters (78.8%) of the participants knew the HIV status of their partners while about a fifth (21.2%) did not know the status of their partners. For partners with known HIV status, the majority (64.8%) of partners were HIV positive while 14% were HIV negative. With

respect to terrain, 64.3% of participants were using urban facilities, 27.1% rural facilities and 8.6% peri-urban facilities. Predominantly (64.3%) facilities were run by Government facilities while CHAL was responsible for 27.1% of facilities.

3.2.4 Clinical Profile

Participants were assessed in terms of duration of ART, dosage of regimen when viral load was taken, total number of drugs taken a day, average adherence in the last 6 months, type of regimen, WHO staging (WHO stage at ART initiation), ever defaulted from ART treatment, knowledge of HIV status before or during pregnancy, completion of 3 adherence sessions, number of staffs in MCH ART corner and DNA PCR of an infant. Table 4 presents the clinical profile.

Table 4: Clinical Profile

Variable	Category	Percent	N
Duration of ART (years)	<1	3.6	15
	1-2	39.0	164
	3-5	47.4	199
	6 and above	10.0	57
Mean		3.16	
Mode		1	
Median		3.00	
Range		0-16	
Has ever defaulted treatment	No	94.5	397
	Yes	5.5	23
Transfer in from other facilities	No	91.4	384
	Yes	8.6	36
Dosage of drugs	1	98.3	413
	2	1.7	7
Total Drugs Taken	1	98.3	413
	3	.7	3
	4	1.0	4
Knowledge of HIV status	During pregnancy	60.2	253
	Before pregnancy	39.8	167
Adherence (%)	<95	17.1	72
	95+	82.9	348
Adherence sessions completed	No	2.4	10
	Yes	97.6	410
WHO staging	1	100.0	420
Type of regimen	AZT/3TC/EFV	1.0	4

	AZT/3TC/NVP	0.5	2
	TDF/3TC/DTG	64.5	271
	TDF/3TC/EFV	33.8	142
	TDF/3TC/NVP	0.2	1
Staff in MCH	1	31.4	132
	2	68.6	288
DNA results of a child	Negative	92.8	337
	Positive	7.2	26

Forty seven percent (47.3%) of the participants had been on ART for between 3-5 years followed by those who had been on ART for between 1 and 2 years at 39%. On the other extremes were participants who had been on ART for less than a year at 3.6% and those who had been on ART for 6 years or more at 10%. According to the mode most participants had been on ART for a year while the mean and median duration of being at ART were 3.16 and 3 years. Looking at all central tendency measures (mean, median and mode) and the range, the distribution of the duration of being on ART is skewed to the left. All participants (100%) were at stage 1 of WHO staging. Single dose regimen was at 98.3% as either TDF/3TC/EFV or TDF/3TC/DTG. Knowledge of HIV status during or before pregnancy was at 60.2% and 39.8% respectively. The majority (82.9%) of participants had an adherence of >95%. The overall positivity rate of mother to child transmission for both 6 and 14 weeks was 7.2% for those continuing with breast feeding period.

3.3 Viral Load Suppression Prevalence by socio-demographic or clinical characteristics

In order to understand the factors affecting viral load suppression and address the second objective to describe factors affecting the suppression of viral load amongst pregnant and breast-feeding women and participants were analysed based on suppression levels by their demographic characteristics as shown in the table below.

Table 5: Viral Load Suppression Prevalence within socio-demographic and clinical characteristics

Variable	Category	Unsuppressed	Suppressed	Chi Square (p value)
Marital Status	Single	70.0	30.0	42.626 (0.000)
	Married	27.5	72.5	
	Separated/Widowed	83.3	16.7	
Age	<25	66.0	34.0	31.027 (0.000)

	25-29	25.1	74.9	
	30-34	32.0	68.0	
	35-39	33.3	66.7	
	40+	43.8	56.2	
Partners HIV Status	Negative	23.7	76.3	75.646(0.000)
	Positive	22.8	77.2	
	Unknown	71.9	28.1	
Terrain of Facility	Rural	33.3	66.7	0.000(1.000)
	Peri-Urban	33.3	66.7	
	Urban	33.3	66.7	
Type of Facility	CHAL	33.3	66.7	0.000(1.000)
	GOV	33.3	66.7	
	Private	33.3	66.7	
	Private-Gov	33.3	66.7	
Duration of ART	< 1	33.3	66.7	20.446(0.000)
	1-2	31.1	68.9	
	3-5	28.6	71.4	
	6+	64.3	35.7	
Adherence (%)	<95	100		173.793(0.000)
	95+	19.5	80.5	
Adherence sessions completed	No	100.0		20.488(0.000)
	Yes	31.7	68.3	
Has Ever Defaulted Treatment	No	29.5	70.5	48.665(0.000)
	Yes	100.0		
Transfer in from other facilities	No	28.4	71.6	49.355(0.000)
	Yes	86.1	13.9	
Total Drugs Taken	1	32.2	67.8	14.237(0.001)
	3	100.0		
	4	100.0		
Drugs dosage	Once	32.2	67.8	14.237(0.000)
	Twice	100.0		
Knowledge of HIV Status Timing	During Pregnancy	17.4	82.6	72.770(0.001)
	Before Pregnancy	57.5	42.5	
DNA Results of a Child	Negative	28.2	71.8	56.012(0.000)
	Positive	100.0		
Type of regimen	TDF/3TC/DTG	1.5	98.5	349.121(0.000)
	TDF/3TC/EFV	90.8	9.2	
Total		33.3	66.7	

Facility terrain and type: No differences were established in terms of the terrain and type of clinic clients were originating from.

Marital status: Women who were married had better suppression rates than those who are single or previously married.

Age status: Participants who were aged below 25 years had lower suppression rates than those above 25 years.

Defaulting and transfers: history of defaulting and transferred from one facility to the other increased the likelihood of non-suppression.

Duration of ART: Women who have been on ART for 3-5 years have higher suppression rates than those below 1 year or greater than 5 years.

Adherence rates and adherence completion sessions: Adherence rates <95% and lack of completion of the first 3 initial adherence sessions increases risk of not being virally suppressed.

Total drugs taken and number of dosages: Frequent dosages and increased number of drugs increased viral load suppression rates.

Knowledge of HIV status during or prior to the pregnancy: Knowledge of HIV status increased suppression rates than those who knew their status prior to pregnancy.

DNA PCR results of a child: All participants whose DNA PCR of their children was positive were not suppressed while 71.8% of their counterparts were virologically suppressed.

Type of regimen: Participants on TDF/3TC/DTG were more suppressed than other drug regimens.

Based on the chi-square statistic, marital status, age and partner's HIV status were the three socio-demographic variables that were statistically associated with viral load suppression. As for clinical characteristics, all were statistically associated with viral load.

3.4 Factors Associated with Viral Load Suppression

In order to identify factors associated with suppression of viral load, all variables which displayed a relationship with viral load suppression at the bivariate level based on the chi-square statistic were entered into the forward stepwise logistic regression model. This will assist to establish the association between viral load suppression and the infant DNA PCR positivity rate amongst breast-feeding women. The odds ratios that a participant was virologically suppressed are presented in Table 6.

Table 6: Logistic regression model- Factors Associated with Viral Load Suppression

Variable	Category	B	Sig.	Exp(B)	95% C.I. for EXP(B)

					Lower	Upper
Age <25 years	25-29	1.327	.002	3.769	1.625	8.742
	30-34	0.923	.043	2.516	1.031	6.138
	35-39	1.139	.033	3.124	1.098	8.887
	40+	2.008	.012	7.449	1.559	35.592
Partner's HIV status Unknown	Negative	1.578	.001	4.848	1.963	11.972
	Positive	1.413	.000	4.109	2.196	7.690
Transfer in	Not a transfer	2.528	.000	12.530	4.153	37.803
Timing of HIV knowledge Before or during pregnancy	During pregnancy	1.537	.000	4.651	2.767	7.817
Constant		-4.620	.000			

According to the odds ratio, age, partner's HIV status, transferring from other facilities and timing of HIV knowledge status were significantly associated with viral load suppression. Women aged 25 years and greater than 40 and above were more likely to be virally suppressed than women younger than 25 years. Women who knew their partners' HIV statuses were more likely to have viral load suppression compared with their counterparts. On the other hand, women who were not transferred from one facility to another were 12.5 (95% CI 4.1-37.8) times more likely to have viral load suppression, compared to those who were transferred. Lastly women who knew their HIV status during pregnancy were 4.7 (95% CI 2.8-7.8) times more likely to have viral load suppression, compared to those who did not know their HIV status before pregnancy.

3.5 Association for infant DNA PCR positivity rate

We also established the association between viral load suppression and infant DNA PCR positivity rate amongst breast-feeding women as shown in tables below

3.5.1 Viral load suppression rates

All breastfeeding women in the study were categorized as either viral load above or below 1000 copies/mL as below table.

Table 7: Suppression rates of breastfeeding mothers

Variables	Number	Percentage
Breastfeeding women with viral load >1000 copies/mL	121	33.3%

Breastfeeding women with viral load <1000 copies/mL	242	66.7%
Total to show all B/F mothers	363	100%

None of the women with viral load less than 1000 copies/mL had a positive child.

3.5.2 DNA Positive results

Since all positive DNA positive results were from viral load levels above 1000 copies/mL, they were grouped together to a value that increases power for analysis. The value of the viral load was those less or greater than 30 000 copies/mL.

Table 8: DNA results of the child by viral load >1000 copies/mL

DNA results of the child by background and clinical variables

Variable	Category	Negative	Positive	Chi Square (p value)
Viral load	<30000	97.6	2.4	62.004(<0.000)
	30000 or more	33.3	66.7	

This study has shown that the higher the VL the higher the risk of HIV transmission. For instance, 66.7% of breastfeeding women who had a viral load >30 000 copies/mL had infants whose results came out positive whilst those who had a viral load between 1000-30 000 copies/mL had 2.4% of infants with positive results.

Chapter 4: Discussions

The chapter will be discussing results established in the study. The main objective of the study was to describe factors contributing to viral load suppression amongst HIV infected pregnant and breast-feeding women who have completed 6 months of ART treatment and association of maternal viral load suppression to infant DNA PCR positivity in Maseru, Lesotho. The study established women's marital status, adherence to ART and completion of adherence sessions were associated with viral load suppression levels. In addition, knowledge of HIV status during pregnancy as opposed to prior to the pregnancy seemed to increase the likelihood of being suppressed. Women who had knowledge of their partners' HIV status and were older than 25 years of age seem to be more suppressed than their counterparts. Furthermore, women who had high viral load increased the risk of HIV mother to child transmission. The chapter will also suggest recommendations for policy makers.

4.1 Viral Load Suppression Rates Prevalence within socio-demographic or clinical characteristics

The overall suppression rates in the study for breastfeeding women were higher at 94.7% than what was found in one study in Kenya with a suppression rate at 78.9% (48). In the study, pregnant women had higher suppression rates at 96.1% compared to breast feeding women at 94.7% even though it was not statistically significant. These findings might be explained by a cohort study in Malawi, which looked at adherence levels for pregnant and breastfeeding women. It reported a lower adherence at 66% in 3 months postpartum period and higher adherence at 73% during pregnancy (43). Post-delivery is stated to also have its own challenges like physical, emotional and economic stresses, with the added burden of caring for a new baby likely contributing to poor adherence (33).

4.2 Factors Associated with Viral Load Suppression

From the conceptual theory of the study, social support had a critical role for adherence and therefore viral load suppression. This study established that women who were married had a significantly higher suppression of viral load than those who were not married. This finding suggests that social support augments adherence through inspiration, assurance, strengthening

and reinforcing of one's aptitude (70). However in a different study, there was no association to adherence and marital status, but limitations on the study was similarities of the homogenous population studied with very little variations in terms of economic and socio-demographic factors which might have masked the importance of marriage as a social support (69).

Adherence has been assumed to be an independent variable towards viral load suppression in the conceptual framework of the study. More findings indicated that women who were not adherent to ART were unlikely to attain suppression of viral load, compared to those who were adherent. This was consistent with other findings(41). The biological plausible explanation of poor adherence is the result of drug dosages below the levels necessitating production of therapeutic effect and therefore enabling existence of drug resistance (64). Furthermore, in this study, women who were on ART for more than 5 years were also stated to be at risk of high viremia in the study as opposed to another study stating 3 years in KwaZulu Natal (66). Some women had reported fatigue in taking their ART and therefore poor adherence (59) leading to viral load non suppression.

We also established that women who had not completed their adherence counselling sessions as indicated on their ART cards were not virally suppressed as opposed to those who had completed their adherence sessions. In Israel, lack of knowledge had been associated with non-adherence (87), similar to Malawi that lack of adequate counselling leads to non-adherence which in turn affects viral suppression (53). Since Option B+, women are initiated on ART after one adherence session and with more mandatory sessions occurring after their ART initiation which can be missed during busy days within facilities. It is therefore important that all women should have the three one on one sessions provided during the initial ART initiation. One study had cited risk factors associated with suboptimal adherence, for women who had transferred from other facilities (53) which the study had similar findings in and therefore should be closely monitored.

In this study, women who knew their HIV status during pregnancy were 4 times more likely to be suppressed than those who knew their HIV status prior to their pregnancy which then reduces the risks of mother to child transmission. One study done in Brazil had similar findings of significant protective factors for mother to child transmission in women who received their HIV positive results during the antenatal care period (50) as they will be virally suppressed. It is

possible that strong emphasis is on mother to child transmission for women who start ART during pregnancy hence the likelihood of being suppressed.

Women who knew their partner's HIV status were found to be more virally suppressed when compared to their counterparts. Disclosure has been demonstrated to be protective for viral suppression as an enhancer of adherence (56) (57). In the current study, women who were aged above 25 years were 3.8 times more likely to be suppressed compared to those below 25 years of age. This was consistent with the study in Kenya as women who experienced plasma virologic failure in the period of 6–14 weeks postpartum had a mean age of 24.2 years in comparison to those aged 27.6 years who were suppressed (48) as the younger age has been associated with cessation of ARVs abruptly (54).

4.3 Association between viral load suppression and infant DNA PCR positivity rate amongst unsuppressed breast-feeding women

In the current study, 6-14 weeks transmission rate for HIV Exposed children was at 7.2%. UNAIDS 2020, has reported Lesotho's 6-week transmission rate of 5% with an end of lactating period of 9% similar to our study findings (25). Lesotho continues to report >5% of transmission rate, above the anticipated WHO target (79) despite achieving the process indicators of ART treatment coverage of >90% (21). This still remains high compared to neighboring countries like South Africa at a final rate of 2%, Swaziland at 3.3% and Namibia at 4.1% (81). Therefore, it is recommended that urgent management of high viral load should be given a priority. Children of mothers who had viral load >30 000 copies/ml were significantly associated with having HIV positive results at 66.7% of their children HIV positive. This was consistent with other studies as mothers who had high viral load had an association with HIV positive infants (80). One study in Malawi established that women on ART with VL >1000 copies/mL were 17 times and those with VL between 40-1000 copies/mL were 9 times more at increased risk of mother to child transmission compared to their counterparts with undetectable VL (88).

4.4 Limitations of the study

The data collected was for women with viral load results and does not allow an opportunity to evaluate the viral load testing rate for pregnant and breastfeeding women in Lesotho. Data was also entered into the MOH database with a single data clerk or record assistant entering multiple indicators, which may have resulted in errors. A mixed approach of qualitative information

would have played a critical role in determining other factors beyond what quantitative data could present. Adherence calculations would have also been beneficial as clinicians fill patients' ART cards routinely without properly evaluating them. Confounders could have also played a role in the outcomes i.e. marital status brings in an added support which unmarried or divorce don't have hence the viral suppression for them.

Option B+ goal has been to promote early initiations of ART in pregnancy which could not be determined from the ART cards the trimester period of initiations in pregnant women as is not indicated on the cards.

Chapter 5: Conclusion and Recommendations

5.1 Summary

Lack of viral load suppression in some women is concerning and signifies a threat to the aim of eliminating mother to child transmission in the country. In order to promote ART retention, adherence and viral load suppression in pregnant and breastfeeding women, it is critical to identify barriers in the attainment of viral load suppression. With recommendations of Option B+, a case management plan that deliberates on individuals plan for disclosure and social support is important to strengthen male partner involvement. Women who had partners with known status were more adherent and virally suppressed than those with unknown status.

There is useful information which identifies indicators which need to be evaluated in women during their pregnancy and breastfeeding period to improve support for them. Adolescents and young women and those transferred in from other facilities will need to be supported more, with frequent counselling and calls from health care providers even outside their visiting days in the clinic. Women who have been initiated on ART prior to pregnancy and those experiencing treatment fatigue after many years have been noted to also be at risk of non-suppression and reinforcement of messages around need to prevent transmission to their infants is important. It is also important to strengthen messaging also pertaining to their health so that they continue to adhere beyond the PMTCT program.

5.2 Recommendation

5.2 Implication to the study for program shifts in Lesotho

It is evident from the study as well that more support is needed by women who are not married as they might not have adequate social support impeding on their adherence. Peer support groups for postpartum women in the communities might be one model that can be used for better support them. Evidence from Sub-Saharan Africa suggests that efforts needed to enhance

retention should be inclusive of addressing acceptance of once status and fear of external stigma which peer support models seems to address (89).

Women who were non-adherent to ART were not virally suppressed. Therefore, non-adherence with use of adherence calculation forms for an objective assessment should be strengthened to identify earlier non-adherence in pregnant and breastfeeding women so that appropriate referrals to psychologists or social workers are done for suitable management. Since those who have been on ART for more than 5 years were established to have high viremia in the study, it is paramount that intensified adherence counselling's are strengthened after every 5 years. Those who would have still attained viral load suppression within each 5-year interval can be recognized and celebrated publicly within facilities as a way of motivation. Close monitoring of completed 3 mandatory adherence sessions for women who are initiated on ART and those who are transferred in from other facilities as were found to also have challenges with viral suppression. Women who have been on ART prior to their pregnancy should also receive intensified counselling emphasizing on MTCT as knowledge enhances adherence (39) because they also struggled with viral suppression.

Women who don't know their partners' HIV status might be struggling with disclosure, therefore health care workers should open a window of opportunity to enquire about disclosure when they encounter such women as it affects adherence. Intimate Partner Violence can also be explored in the discussions as is associated as the main cause of non-disclosure in relationships (90). Subsequently, younger women below the age of 25 years had challenges with viral suppression and reinvigoration of group sessions beyond individual sessions through peer support groups for motivation (85) can go a long way.

If Lesotho is to achieve a mother to child transmission rate of <5% at end of lactating period, it is recommended that a high viral load of any pregnant and breastfeeding should be promptly attended to for urgent management (91). Currently, Lesotho does not do mandatory baseline viral load testing for any HIV positive women on ART during their first ANC (7), therefore it is important that the policy shift is made in this direction. This will allow corrective measures to be done on time for high viral load management and prevent MTCT (91). In addition to baseline viral load testing as previously alluded to, countries like South Africa with end of breastfeeding transmission rate of 2% (25) have adopted a one-month viral load monitoring interval after the 1st

encounter of high viral load in pregnant and breast-feeding women (91) different from Lesotho where 3 months viral load monitoring is still maintained (17). This enables prompt switching of a regimen if there is no improvement in the log difference of the two consecutive viral load results despite enhanced adherence counselling for ART optimization. It is therefore crucial that such shifts are done as well in the country.

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Appendices

Appendix 1: Plagiarism Declaration

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Ruseletso Maja (Student number: 1606116) am a student registered for the degree of MPH (MCH) in the academic year _____.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: _____ Date: 25/10/2020

Appendix 2: Check-list

Research Topic: Factors Contributing to Viral Load Suppression among Pregnant and Breastfeeding Women on Antiretroviral therapy in Lesotho

Variables	**Response for Case no**												
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**
Facility name													
Date of birth													
Status (Pregnant or breastfeeding)													
Viral load													
Age (years)													
Marital status													
Partner's HIV status													
Terrain of facility accessing ART													
Type of Clinic accessing ART													
Duration of ART													
Average adherence Art calculation in the last 6 months													
Dosage of regimen													
Total drugs taken in a day													
Type of regimen													
WHO clinical staging at ART initiation													
Transfer in from other facilities													
Has ever defaulted treatment													
Knowledge of HIV status													
completion of 3 adherence sessions													
Number of staff in MCH ART corner													
6. DNA PCR of infant													

Appendix 3: Code Book for Variables

Variable	codes
Date of birth	enter as given e.g. 1953
Status (pregnant or breastfeeding?)	1 breastfeeding; 2 pregnant
Viral load	enter the provided info
Age	this will be calculated from date of birth
Marital status	1 single; 2 married, 3 divorced, 4 widowed
Partner's HIV status	0 negative 1 Positive 2 unknown
Terrain of facility accessing ART	0 rural 1 peri-urban 2 urban
Type of Clinic accessing ART	1 GOV 2 CHAL 3 Private 4 Private-Gov
Duration of ART (years)	Enter 0 if less than a year
Average adherence Art calculation in the last 6 months	Enter the provided response
Dosage of regimen	1 once 2 twice
Total drugs taken in a day	Enter provided response
Type of regimen	Enter provided response
WHO clinical staging at ART initiation	Enter provided response
Transfer in from other facilities	1 yes 2 no
Has ever defaulted treatment	1 yes 2 no
Knowledge of HIV status	0 during pregnancy 1 before pregnancy
completion of 3 adherence sessions	Enter provided response
Number of staff in MCH ART corner	Enter provided response
DNA PCR of infant	0 negative 1 Positive

Appendix 4: Ministry of Healthe ethical clearance

Ministry of Health
PO Box 514
Maseru 100

LESOTHO

Category of Review:
[x] Initial Review
[ ] Continuing Annual Review
[ ] Amendment/Modification
[ ] Reactivation
[ ] Serious Adverse Event
[ ] Other

REF: ID30-2020

Date: May 08, 2020

To
Puseletso Maja
University of the Witwatersrand

Dear Dr Maja,

RE: Factors contributing to viral load suppresion amongst pregnant and breastfeeding women on antiretroviral therapy in Lesotho.

This is to inform you that the Ministry of Health Research and Ethics Committee reviewed and APPROVED the above-named protocol and hereby authorizes you to conduct the study according to the activities and population specified in the protocol and data extraction from data systems. Departure from the approved protocol will constitute a breach of this permission.

This approval includes review of the following attachments:
[x] Protocol
[x] English & Sesotho informed consent form
[x] Data collection tools in English
[J Participant materials [insert types, versions
[x] Other materials: CV of the PI, request letter for approval

This approval is VALID until May 10, 2021.
Please note that an annual report and request for renewal, if applicable, must be submitted at least 6 weeks before the expiry date.

All serious adverse events associated with this study must be reported promptly to the MOH Research and Ethics Committee. Any modifications to the approved protocol or consent forms must be submitted to the committee prior to implementation of any changes.

We look forward to receiving your progress reports and a final report at the end of the study. If you have any questions, please contact the Research and Ethics Committee at rcumoh@gmail.com (or) 22226317.

Sincerely,

DR. Nyane Letsie

Director General Health Services

DR. Llang Bridget Maama-Maime
Member, National Health Research Ethics Committee (NH-REC)

Appendix 5: WITS Ethical Clearance

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Puseletso Maja

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M200313

NAME: (Principal Investigator)	Dr Puseletso Maja
DEPARTMENT:	School of Public Health Ministry of Health Maseru, Lesotho
PROJECT TITLE:	Factors contributing to viral load suppression amongst pregnant and breast-feeding women on antiretroviral drugs in Lesotho
DATE CONSIDERED:	27/03/2020
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Juliet Nyasulu
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	08/06/2020

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions.Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report.** The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **March** and will therefore be due in the month of **March** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES