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Factors associated with Viral load detectability among HIV-infected pregnant women in a high prevalence region in Rwanda

A research dissertation in partial fulfilment of the requirements for the degree of

MASTER OF PUBLIC HEALTH

By

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Dedication

This thesis is dedicated to my supervisor, entire family and friends who encouraged me during my studies and colleagues who indirectly contributed to the completeness of this work.

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Abstract

Background

Globally almost 18 million HIV infected are women of reproductive age, with about 1.4 million pregnancies occurring annually to women living with HIV. In Rwanda, HIV infection prevalence is higher among women (3.6%) than men (2.2%) and ranges from 2.8 to 2.9% in 2015 among pregnant women .While Viral suppression for the general population has been estimated for Rwanda to be at 91% in 2018, frequent VL monitoring is recommended for HIV infected pregnant women but there is little or none existing data on viral load monitoring and suppression among pregnant and postpartum women. We used existing data from the International Epidemiology Databases to Evaluate AIDS (IeDEA) to determine socio demographic, medical characteristics and obstetric profile of HIV infected pregnant women newly on ART, determine the proportion of new enrolled HIV positive pregnant and post-partum women with a detectable VL at six months post ART initiation and identify factors that are associated with a detectability of VL during this period.

Methods

The study was a cross-sectional study design that included HIV positive pregnant and postpartum women newly enrolled in HIV program from July 2016-June 2018 in Kigali City. For data analysis, we used an IBM SPSS Statistics version 2, predictor variables such as socio demographic, medical and obstetric features were described using frequency and percentage whereas VL detectability as an outcome of interest was described using a pie chart diagram. Chi square test was used to generate association between individual predictors and outcome of interest. Multivariable analysis using logistic regression model was performed to check out the strength of associations.

Results

Of 310 study participants, who were enrolled to HIV care while pregnant or postpartum , the mean age was 31.3 years and the median gestational age was 21 weeks at Enrollment. Of these women,98% (n=305) had a viral load check, 82% (249) had undetectable viral load compared to 18% with detectable viral load using a cut-off of <=20 copies/mL of plasma. Of these with a detectable VL, 7.5% (n=23) had a viral load > 1000 copies/ml of plasma. Factors such as age category (P-value = 0.018) and viral load category (P-value 0.000) were found to be more likely associated with viral load

detectability during pregnancy and postpartum. At multivariable analysis, there was no much evidence that socio demographic features, nor medical features or obstetric factors that were associated with VL detectability during pregnancy or post-partum period. Similarly, Silveira et al, 2002 revealed that there was no evidence that an individual clinical status would explain the undetectability of VL.

Conclusion

Our findings indicate an overtime increase of VL measurement among HIV-infected pregnant or postpartum women which highlights the success of the Rwanda HIV treatment and prevention program. Nevertheless, MTCT remains a concern since 18.36 % had a detectable VL and of these 7.5 % failed to suppress their VL < 1000 copies/ml. Based on findings for this study, factor associated with VL detectability during pregnancy or postpartum period are highly needed to be more explored.

Key words: HIV,Viral load, detectability

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List of abbreviations

ANC: Antenatal care

ART : antiretroviral therapy

CD4: cluster of differentiation 4

CI: Confidence interval

DNA: Deoxyribonucleic acid

ER-RCBP: Einstein Rwanda and Research Capacity Building Program

HIV : Human Immunodeficiency Virus

HAART: Highly active antiretroviral therapy

HTS: HIV testing services

IBM SPSS: Statistical Package for the Social Sciences

IeDEA: International Epidemiological data Base to Evaluate Aids

MTCT: Mother-to-child transmission

NCI: National Cancer Institute

OR: Odd ratio

PIs: Proteinase inhibitors

PCR: Polymerase Chain Reaction

PLHIV: Person living with HIV

PMTCT: Prevention of mother-to-child transmission

RNA: Ribonucleic acid

STD :Sexual transmitted diseases

USA: United States of America

VL : Viral load

WHO: World health Organization

Chapter One . Introduction

1.1. Definition of key concepts

Human Immunodeficiency Virus (HIV) : The HIV virus is transmitted via human vital fluids and attacks the host's defense system, especially the cluster of differentiation 4 (CD4)cells, called T cells. As time goes on, this virus can damage many of these cells that the host' s antibodies can't fight off, then after infections take place (1).

Viral load (VL): The term used to define the amount of HIV in your blood, the results of a VL test are defined as the number of copies of HIV ribonucleic acid (RNA) in a millilitre (ml) of blood. VL measure offers information of the risk of HIV transmission and also become an indicator of treatment(2).

Detectable Viral Load: The term is used if VL hasn't dropped to undetectable levels for a period of three to six months of initating HIV treatment. For the purpose of this analysis and given the approved definition of this term into Rwanda National Guidelines for HIV treatment and prevention ,Edition 2016, we shall use the term to mean VL greater than 20 copies/ml after six months of starting HIV treatment while pregnant or during post-partum period(3).

1.2. Study context

This study used a dataset from a program called Einstein Rwanda Research and capacity Building Program (ER-RCBP) which host the International Epidemiological data Base to Evaluate Aids(IeDEA) among other projects, coordinated through a partnership between the Albert Einstein College of Medicine,USA and Various institutions in Rwanda that include Rwanda Military Hospital (RMH) the implementing institution, University of Rwanda,We-Act for hope, Masaka District Hospital,Cartas,Kigali Archdiocese among others. IeDEA gathers HIV/AIDS routine data from seven regional across the globe, including four in Africa.

Rwanda IeDEA is part of the central Africa IeDEA region, it started in 2011 as longitudinal study, it collects HIV/AIDS data from ten health facility both located in kigali City ,of these eight are public

health centres, (Betsaida, Busanza,Gahanga,Gikondo,Kabuga,Kicukiro,Masaka and Nyarugunga) one is a private health center (We Actx) , and another one is a referral hospital (Rwanda Military Hospital) and this is the implementing institution. Funds are provided by the National Cancer Institute (NCI) since 2007.

1.3. Background

Globally almost 18 million HIV infected are women of reproductive age, the percentage of infections happening in female is cumulative for various advanced nations. Female are predominantly vulnerable to HIV infection for social, biological and cultural causes(4) About 1.4 million pregnancies arise yearly to women living with HIV (5). In southern part of Africa region, the HIV in pregnant women is over 30% of prevalence, and rates of incidence are rising in south-east Asia(4). Most of observed HIV cases, 70% are attributed to sexual acts with opposite sex transmission , above 90% of infections in children are attributed to vertical transmission.

In Rwanda, estimates of HIV infection prevalence are at 3% in general population, higher in women versus men (3.6% Vs 2.2%) (6). Recent estimates among pregnant women, range between 2.8 - 2.9% in 2015 (6).

Rwanda has a highly successful HIV program. In April 2012, the Rwandan government began a policy of lifelong ART for prevention of mother-to-child transmission (PMTCT) irrespective their CD4 measurement or clinical profile (Option B+). Rwanda has almost reached universal coverage of PMTCT, and transmission level of HIV through mother-to-child transmission (MTCT) has substantially diminished, 1.58% (95% CI 1.05–2.37%)(7). Rwanda was also one of the first African countries to adopt and implement universal antiretroviral therapy (ART (i.e,Treat All) as a national policy in July 2016. Following the adoption of Treat All, ART coverage has increased nationally, from 74.7% in July 2016 to 82.6% in June 2017 (8).

Defined by the Rwanda Ministry of Health as viral load ≤ 20 copies /ml for at least two consecutive tests (9), viral load (VL) suppression after ART initiation is the best health intervention to positively change the wellbeing of HIV infected pregnant and thus avert both sexual and MTCT (10). Individuals who are adherent to their antiretroviral (ARV) regimen generally attain viral suppression

between 12 to 24 weeks' time after the initiation of treatment (11), however, pregnant women with advanced viral loads and worsened CD4 cell measurement at ART initiation are likely to take much time to attain viral suppression. In addition, poor ART adherence is thought to result in failure to achieve viral suppression during pregnancy or the postpartum period for approximately one-third of pregnant women who starts ART during pregnancy (5).

More repeated viral load checks is suggested for HIV infected pregnant women versus to non-pregnant individuals because of the importance of rapid and continued viral suppression in preventing HIV transmission during pregnancy (12). However, there is little data available on viral load monitoring for pregnant and postpartum women in limited resources countries (13).

Government of Rwanda's HIV treatment program guidelines of 2013 and 2016 recommended VL testing for pregnant women after six months post ART initiation and current guidelines (2018) recommend VL testing for newly enrolling HIV infected pregnant women at three months post ART initiation and every 6 months during pregnancy and the postpartum period. VL was considered to be suppressed in both 2013 and 2016 Rwanda National Guidelines for Prevention and Management of HIV and STIs once ART reduces an individual VL to an undetectable level. This level is less or equal to 20 copies /ml (9) for at least for two consecutive VL tests.

Moreover, while viral suppression for the general population has been estimated for Rwanda—ranging to be at 91% in 2018 (6), there is little data on viral detectability for pregnant and postpartum females, or on factors associated with none attaining undetectable level viral load in this population. By addressing this gap, we used Rwanda data from the IeDEA to examine the proportion of new enrolled HIV infected pregnant women having viral load checks post ART initiation, the proportion of those who are virally suppressed/unsuppressed, and factors associated with VL detectability following ART initiation.

1.4. Problem statement

HIV infected pregnant women require ongoing treatment and thus consistent VL suppression monitoring to control their illness and survival .Frequent VL measurement is suggested for HIV infected pregnant women but no data exist on VL checks practices and VL suppression among this population.

There are problems related to adherence to ART in this population and many studies have revealed significant levels of less engagement from HIV care among postpartum women but data related to VL control among women who initiated HIV treatment while pregnancy are inadequate(14).

Few studies have reported on VL suppression and factors that are associated with it among adult HIV positive individuals on ART in Rwanda where ART is provided to Person living with HIV (PLHIV) irrespective of CD4 cell measurement. To our knowledge, none have examined these factors among study population and yet MTCT remains a concern in Rwanda.

The Rwanda target of Viral load suppression is at 90% in 2018, and 95% in 2020 for general population on ART (15) but there is no specific set targets to HIV infected pregnant women. The gap seems to be that even though Rwanda guidelines specify VL monitoring every 6 months for pregnant women(3), no data exist at country level as to how often it is really happening . This study will be among the first to examine these factors in our country and will provide important insights about VL monitoring practices following the adoption of Treat All as national policy. The results from this study will also help to inform strategies to reduce vertical HIV/AIDS transmission.

1.5. Purpose of the study

With limited information about VL monitoring in HIV+ pregnant or postpartum women in countries with scarce resources that includes Rwanda , it is with a great important to evaluate the actual practices of VL checks post ART initiation and address the associated factors with VL detectability among this population. This study will inform the National HIV treatment and monitoring guideline direction towards VL checks practices and strategies to reduce vertical HIV/AIDS transmission.

1.6. Research Objectives

The general objective is to determine the VL checks practices and linked factors with VL detectability among new enrolled HIV infected pregnant and post-partum women in Rwanda.

1.6.1.The specific objectives

1. To describe socio demographic, medical profiles and obstetric features of HIV infected pregnant women on ART in high HIV prevalence region in Rwanda
2. To determine the proportion of new enrolled HIV infected pregnant women with a detectable VL after six months post ART initiation in high HIV prevalence region in Rwanda
3. To identify socio demographic, medical and obstetric factors that are associated with detectable VL during pregnancy or post-partum period.

1.7. Research Questions

The above specific objectives respond respectively to the following research questions:

1. What are socio demographic medical profiles and obstetric features of HIV infected pregnant women on ART ?
2. What is the proportion of new enrolled HIV infected pregnant women with a detectable VL after six months post ART initiation ?
3. What are factors linked with detectable Viral load during pregnancy and post-partum period?

Chapter two: Literature Review

HIV infection is spread via inanimate contaminated prick needles, un protected sexual acts with an HIV+ partner, during pregnancy,labor,delivery or breastfeeding period, or during transfusion. This infection fallouts from modification of genetic code of susceptive cells(16).

Once infected, the resulting provirus may stay inactive for some time. This dormancy period pays to the variability perceived in dormancy to the sickness itself. The cause of vigorous copying after a period of dormancy is presently not known. After viral reproduction starts, the host cell deceases.

After certain period, CD4 cells turn to low level and defense function is reduced. Reduced immune function cause proliferation of those microorganism that lived in human but not cause any harm and leads to other infection. Severity of infection is measured through CD4 levels. These together with VL are used as a base of treatment and prophylaxis measures. The VL in blood starts to reduce after the body starts a comeback to fight it. This process is called clinical dormancy, nevertheless the virus duplicate over time therefore advanced deterioration of CD4 T lymphocytes. This era can take 10 years even higher. After this period, the virus may any more be controlled and proliferation in viral load take over (16). This change is often complemented by an AIDS outlining illness such as Kaposi’s Sarcoma.

The decrease in MTCT of HIV is considered as the most actual public health creativities across the world. In the nonexistence of preventive actions, the risk of MTCT would be between 25-30%. Introduction of HIV testing and antiretroviral medication, delivery by cesarean section prior to onset of labor, and discouraging breastfeeding, the MTCT has lowered to < 2% in the United States, to <1.9 % in Rwanda(17)

2.1. Burden of HIV in pregnancy

From Global Burden of Disease perspective in 2015, HIV/AIDS was mostly attributed to death occurred in women of childbearing age worldwide. Estimations vary on specific context like in sub-Saharan Africa 25% of pregnancy-related deaths were attributed to HIV and AIDS versus 5% worldwide and mothers infected with HIV were at 6-8 times higher risk of dying while pregnancy or postpartum compared to their HIV-negative peers(18).

2.2. Pregnancy and HIV history

In pregnancy, human defense function is repressed in HIV+ and none HIV infected but pregnancy its self does not cause any effect on the normal history of HIV infection in women, though this infection is a leading cause of maternal death in specific regions. As the epidemic progresses, some opposing pregnancy effects have reported in HIV+ women with advanced disease(19) but two different studies conducted in New York, revealed a none statistical significant difference in spontaneous abortion rates in HIV+ versus to none HIV- women and HIV has not been confirmed to change pregnancy results(20). Initially it was thought that the mixture of pregnancy and HIV infection could hurry the development of the disease since pregnancy has traditionally been deliberated as an immunosuppressive state. To day, the influence of pregnancy on HIV viral loads has been assessed in few studies, but generally a big number of women in these studies had greater viral loads six months after delivery compared to pregnancy period(21).

HIV related infections that happen in pregnancy are due to the stage of HIV disease and level of immunosuppression not for the pregnancy itself. Pulmonary infections such as pneumonia might be much in pregnant women and remain a serious cause of maternal death, followed by mechanical

issues due to compression of the diaphragm (22). Some reports indicated that pregnancy-linked infections such as vaginal candidiasis and urinary infections happen at greater proportions and with greater severity in the location of HIV infection, but these information have not been verified.

2.3. Epidemiology of HIV

They are only three means for HIV transmission, unprotected sex acts; blood products, or from MTCT .Almost 70% HIV infections are outcome of MTCT .

Generally, every seven days, about 6,200 early aged women between 15–24 years converted into HIV infection .In sub-Saharan Africa, 4-5 new HIV cases are in female aged 15–19 years. Girls aged 15–24 years have a two times risk to be living with HIV compared to their brother's males. Almost one third (35%) of female worldwide had physical and/or sexual violence at some point of time in their life and these acts put them on 1.5 times risk of acquiring HIV compared to female that never had such sexual harassment. Worldwide ,in 2018 almost 82% of pregnant women living with HIV had access to ART to prevent transmission of HIV to their child (23)

In Africa, the predominant mode of spread of HIV is heterosexual; the Southern Africa is the most affected region. In Kenya, Malawi, Namibia, Rwanda, South Africa, Tanzania, Zambia and Zimbabwe around 10% of females attending prenatal clinics in urban areas are HIV+ (4)

2.4. Vulnerability of women to HIV infection

Female living in the emerging countries are at higher hazard of HIV infection compared to male for a different factors.

2.4.1. Factors related to biological effect

Sexually and urinary tracts transmitted diseases are many in some African nations, ineffectively cured or "with no signs and symptoms" STD illness in female may be a key factor in female living with HIV .Vulvar, vaginal irritation or lesions may enable entrance of the virus. In Zimbabwe, female susceptible to a background of genital lesion and pelvic irritative disease were 6 times more likely to be HIV+. Although the evidence is not yet settled, relations between modern contraceptive use and increased HIV risk have been described.

2.4.2. Factors related to Socio-cultural

Gender imbalances, low economic level, inaccessibility to education and privation of occupation opportunities generating income push a number of females into profitable sex acts in order to live, which put them at great hazard of being infected with HIV. On the other hand, many women are faithful, but sexual behavior of their male partner put them at great risk. The wish or the societal force to reproduce put much pressure to female to do protected sex. Early aged female are at great hazard of infections in emerging nations at the commencement of their procreative life. More often after being diagnosed for HIV, many female will not modify their procreative selections. Feminine barrier methods continue to be costly or inaccessible in many emerging countries, where man resistance to condom practice is like a habit, though the latest inauguration of female condom social marketing in certain Southern African countries has proven a substantial demand(24).

2.5. Pregnancy and HIV infection effect

This infection has traditionally stated to have slight upshot on gravidity result or difficulties but it is hard to determine its contribution against drug use during pregnancy and poor prenatal care to adverse results in these women .Some studies reported that HIV can be an uninterrupted basis or

indicator of a composite interface of connected medical profiles and social conditions that shake pregnancy while other findings have revealed a lack of relationship (25).

Complications of pregnancy have been linked with HIV infection in numerous findings whereby in a study conducted in Sub – sahara African countries, HIV+ female had 1.47 risk times to have had spontaneous abortion, and this risk was increased to 1.81 in Uganda (26). Ectopic pregnancy have been highlighted in HIV+ female compared to uninfected ones which may be connected to the effects of additional coexisting STDs.

2.6. Features affecting MTCT of HIV

These are features that can increase risk for passing on HIV to your baby, they may occur:

2.6.1. During pregnancy

Whereby having an HIV-linked disease, like pulmonary infections, having a big amount of HIV viral load, having a STDs, poor adherence to ART and using leisure drugs, particularly injected drugs, during pregnancy may affect MTCT in one way or the other. In one of all these conditions, an individual should have a sexual health screening if you are HIV infected when you are pregnant, especially when you are primigravida(27).

2.6.2. Throughout delivery

When your amniotic liquids breach four or more hours before delivery or if you have a premature baby, having untreated STDs when you give birth, or you have a detectable viral load they raise the risk of passing HIV to your baby for case of vaginal delivery compared to caesarean section(27,28).

2.6.3. After delivery

If you are a breastfeeding mother, to escape transmissing HIV to your baby, it is safer to none breastfeeding methods such as formula feed because breast milk can enclose infections. Inquire the healthcare provider team all necessary information and how to behave and keep your confidentiality if a colleague or an associate family member want to know the reason why you are not breastfeeding.

2.6.4. Viral load

The probability of transmission is higher when there is a high level of maternal viraemia, with the increase of innovative procedures for the virus quantifications, like quantifiable Polymerase Chain Reaction (PCR) DNA and RNA.A connection between the mothers viral load and the hazard of passing virus to child has been verified. Example is that among women with VL >50 000 RNA copies/ml of plasma during delivery period 50% transmit virus to their children.

The French study revealed that transmission rates increased with cumulative viral load,12% for those with < 1000 copies/ml versus 29 % in those with > 10 000 copies/ml(24). Few studies have revealed that HIV transmission can happen at low VL level, for causes which are not known, but perhaps reflect the various effects acting on MTCT. The virus in vaginal discharges or breast milk are significant factor of passing risk while pregnant or after delivery.

In Rwanda, post-delivery transmission was found to be connected to the existence of HIV-1 infected cells in breast milk(29).The existence of STDs or other reasons of irritation, vitamin A shortage and local human defense response can disturb virus changes.

People adhering to their ART regimen, who do not experience any resistance to the prescribed drug should attain undetectable viral level in 12 to 24 weeks. VL checked in HIV infected pregnant individuals should be done at the primary hospital visit, 2-4 weeks after commencing or shifting ART, once-a-month till undetectable level, and at least every three months period afterwards(12).

VL measurement while on ART is vital for individuals to improve clinical outcomes and public health level to allow for programme surveillance.

Likewise, pregnancy can disturb the drug exposure levels or effectiveness of some drugs; women taking these drugs can require a shift in therapy or extra measurement of VL. Pregnancy rises the hazard of glucose intolerance protease inhibitors (PIs) ,have been linked with increased hazard of high sugar in the blood, diabetes mellitus or exacerbation of existing disease. Female with HIV on ART while pregnancy should be screened for glucemia at 24-28 weeks' of pregnancy (30)

2.6.5. Viral load measurement in pregnancy

Known that increased VL is the highest risk for MTCT, a strong emphasize should be for frequent VL checks while pregnancy or post-delivery and this practices have been a ten years long standing culture in resourced states (31)

Nevertheless, some intenational guideline such world health organization,edition 2013 did not provide difference of VL checks in pregnancy as opposed to general population . Besides that various female in emerging states, register late for prenatal care and thus many HIV+ female start ART in late term of pregnancy, subsequent routine guidelines, a big number of these women would give birth prior to first VL check at six months or those who conceive while on ART might not be qualified for their annual VL check before giving birth. In a Cape Town, 35% of female registering in prenatal care were on ART(27) . While female on ART prior to pregnancy were previously been assumed to be virally suppressed during their pregnancy but, Myer et al. (2014) indicated that 24% of those one on ART in a public sector clinic were not virologically suppressed at their first vist of prenatal care; 13% of these women had a VL>1000. These ones may have evaded ART entirely, poorer adherent to ART, acquired resistance to ART or have experienced virological failure. Many researchers concluded that 'the lack of routine viral load check during prenatal appointment resulted in a failure to discover women who had defaulted ART before to or while pregnancy'or discover those who are at great risk of having higher VL on time(28)

VL measurement in pregnancy is not clear across the world and time to achieve viral suppression in pregnancy need to be short to enable prevention of MTCT, therefore it is exceptionally vital to timely check VLs pregnant female newly initiated ART, as well as those who were already on ART to offer a chance of achieving virological suppression before delivery .These shall be done by strengthened adherence support, re-initiation of ART in those who completely abandoned, or shift of ART regimens in cases of treatment failure . In this case, infants at high risk of in-utero transmission shall be identified on time and potential influence decisions about infant feeding and prophylaxis shall be taken in advance.

VL suppression post ART initiation is a best medical intervention to increase the wellbeing of HIV infected pregnant mother to avert both sexual and MTCT. The commonest issues faced by HIV country programmes is at what time and how frequent VL would be checked in HIV infected

pregnant cascade and yet WHO highlighted that during labour period and delivery as a high risk for MTCT(5). However predictions of VL suppression among pregnant women initiating ART at these particular periods is not well known.

2.6.6. Factors related to obstetric

Obstetric factors are imperative determinants of HIV transmission to child. the French perinatal cohort study revealed that: "preterm delivery, bleeding during pregnancy ,prolonged rupture of membranes and obstetric procedures were linked to HIV transmission risk"(24). The American study revealed that : " period of ruptured membranes of over four hours approximately doubled the hazard risk of infection, irrespective of the eventual way of delivery" (32).

2.6.7. Maternal nutritional factors

Numerous micronutrient shortages, increased micronutrient wants while pregnant, poor absorption due to infections, pay to the development of nutrient scarcities and probably reduces the human ability of defensive system there after occurrence of additional infections or results in wasting. Individuals infected with HIV, though, tend to accrue iron in tissues, especially bone marrow, the brain, muscle, liver, and spleen. Even if it yet confirmed, preliminary findings e indicated that larger amount of iron stores result in a quicker progression of HIV infection (33). Low levels of B_{12} may be linked with progress to AIDS.

2.7. Health interventions to prevent HIV for pregnant mothers

The prevention of novel infections in motherhood age ruins a vital section. This comprises the decrease of mother's susceptibility to HIV infection over enhancement of mother's stands in the community, the provision of facts about HIV/AIDS and its avoidance, raise of protected and safe sex, and suitable treatment for STDs

A various number of probable health interventions have been suggested or are under examination, but the only verified to be operational in reducing MTCT of HIV as per today is the use of ART and the avoidance of breastfeeding. This use in motherhood period should be well-thought-out for two major reasons: the wellbeing of infected woman and avoidance of transmission to the baby.

2.7.1. PMTCT as an overall prevention of MTCT of HIV

In a communities whereby breastfeeding is a mutual practice comparable to Rwanda, the likelihood of passing HIV from the mother to her child is more likely high in the nonexistence of avoidance interventions. Likelihood of passing HIV varies between 20-45% in general,5-10% during pregnancy, 10-20% while giving birth and 5-20% post-partum. In advanced states where PMTCT programs are well executed and where the most effective ART is delivered to HIV-infected pregnant women with stopped breastfeeding, the level of MTCT for HIV is < 2% at 18 months (17)

The PMTCT program is grounded on an inclusive four-pronged approach: "Primary prevention of HIV infection among women in childbearing age, Preventing unintended pregnancies among women living with HIV,Preventing HIV transmission from women living with HIV to their infants and Providing suitable treatment, care and support to mothers living with HIV, their children and families HTS is recommended for pregnant women as a crucial component of the package of care in all antenatal services"(17). In Rwanda, entirely female attending the first prenatal visit are tested for HIV and their partners,

2.7.2.Post-delivery care

The delivery care is a health services provided in postpartum period and these services do not require distinct nursing facilities and should be alike in bot HIV+ as well as in HIV- . Some of HIV+ female may require private facilities to reduce the social stigma connected with not breastfeeding if opted for. HIV + women are more likely to be exposed to postpartum infections compared to their peer's sisters. Health care providers should be conscious of these complications and provides skills on the warning sign of infection at the time of discharge, especially where post partum hospital stay is short .

Chapter three. Methodology

3.1. Study design

This was a cross-sectional design that used quantitative approach. Descriptive and analytic methods were applied.

3.2. Study Setting

As a study setting, this was carried out in Kigali city where there is an increased prevalence of HIV(34). The selected health centers were the ones having PMTCT services whose their data are captured under IeDEA network database (refer to study context).Each health center routinely capture HIV related data into OpenMRS software, and from this data are uploaded to the IeDEA network server.

This network consist of ten health facilities, including one private health center (We-Act), one hospital (Rwanda Military Hospital(RMH)) and eight public health centers (Bethsaida, Busanza, Gahanga, Gikondo, Kabuga, Kicukiro, Masaka, Nyarugunga).

Two of these health facilities are not offering PMTCT services , RMH and We-Act, therefore only eight sites were considered in this study.

3.3.Study Population

The study participants were all newly enrolled HIV infected pregnant women ,from July 01,2016 to June 30, 2018 ,aged between 15-49 years.

3.4.Sampling and Sample size

The study included all newly enrolled HIV infected pregnant women into PMTCT program at eight health centers located in Kigali city under the IeDEA network database.

The HIV guideline that inspired our study started on 1st July 2016 and ended on 30th June 2018 (after this date the guideline changed). All eligible subjects enrolled in the programme during this period were included in the study. The concerned total population under this study was 310 women distributed as follows:

Table 1.Distribution of study participant per IeDEA site

Variables	Frequency	Percentage
Newly enrolled pregnant women per site (n=310)		
BETHSAIDA	8	2.6
BUSANZA	54	17.4
GAHANGA	48	15.5
GIKONDO	8	2.6
KABUGA	52	16.8
KICUKIRO	31	10.0
MASAKA	68	21.9
NYARUGUNGA	41	13.2
Total	310	100

Source: Data analysis

3.4.1. Inclusion Criteria

All newly enrolled in HIV-infected pregnant women, ranging between 15-49 years old who initiated ART during pregnancy whose data were available in IeDEA database from July 01,2016 to June 30,2018

3.4.2. Exclusion Criteria

Women who got pregnancy while on ART, HIV infected women enrolled to HIV care before July 01,2016 or after July 31,2018 and not meeting the specified age were excluded .

3.5. Data collection methods and procedures

We developed a list of variables that we felt that could respond to our research objectives using the IeDEA data dictionary, then we submit the list of variables to the IeDEA data management team to abstract and give us a complete dataset.

3.6. Specification of variables

In this study, the followings were predictor and outcome variables under consideration

Table 2.Study variable list and their definitions.

Variable	**Names of measures**	**Definition**	**Variable(s) required from IeDEA**
Eligibility	1.Method of enrollment 2.Pregnancy status 3. Female	1.HIV care entry point = PMTCT 2. Women who were pregnant when enrolling into HIV care	1.HIV care entry point 2. Pregnancy status (Coded response: Is the patient pregnant?) and corresponding date of observation 3 Admission date 4 Enrollment date 5. Sex = Female
Outcom	Detectable Viral Load	VL greater than 20 copies/ml after two	The amount of copies/ml of DNA/RNA in patients

Variable	Names of measures	Definition	Variable(s) required from IeDEA
e	(Categorical variable)	consecutive VL tests post ART initiation	with HIV: 1.Number of Viral load checks from July 2016-June 2018 2.Viral load values per check 3.Viral load date per check
Predictors	Social demographic and economic status	1.Age: Patient's age in years at time of enrollment into HIV care (derived from birth date and enrollment date) 2.Marital status 3.Profession	1.Mother's date of birth and enrollment/admission date 2.Civil status/Etat matrimonial 3. Employment type
	HIV diagnostic time	When a mother has been confirmed to be infected with HIV	Diagnosis date
	HIV status disclosure	Mother disclosed her HIV status to anyone	1.Disclosed 2.Undiclosed
	ART initiation time	When a mother started anti retroviral treatment/drug	Antiretroviral treatment started date
	Gestation age at enrollment	Number of weeks or months the mother has been pregnant or Pregnancy age (in weeks)	Date last menstrual period Expected date of delivery Age gestation (week of the current pregnancy at time of entry into care) Date of delivery
	Obstetric history/ information	1.Gravidity (number of times a woman has	1. Gravidity and respective date of

Variable	Names of measures	Definition	Variable(s) required from IeDEA
		been pregnant) 2. Excessive vomiting during pregnancy (Hyperemesis gravidarum) 3.Other gynecological & obstetrical history information 4.Obstetrical complication 5.Gestational diabetes	observation 2. Hyperemesis Gravidarum and respective date of observation. 3Other gynecological and obstetrical history and respective date of observation 4. Obstetrical Complication Other and respective date of observation 5. Gestationnel diabetes respective date of observation
	Antenatal complications	1. Laboratory test for albumin in the urine 2. Fluid accumulation in the lower limbs 3. Body Mass Index (BMI), measured/calculated 4. Vaginal Bleeding	1. Urinary albumin = yes and respective date of observation 2.Edema = yes and respective date of observation 3.BMI and respective date of observation 4.Vaginal bleeds
	WHO stage at enrollment	Assigned WHO HIV stages at enrollment	WHO stage WHO stage date
	Chronic diseases at enrollment or during pregnancy time	Diabetes: Diagnostic Diabetes=yes	1. Any type of: Diabetes and respective date of

Variable	Names of measures	Definition	Variable(s) required from IeDEA
		Hypertension: Diagnostic Hypertension = Yes Asthma: Diagnostic Asthme=Yes	observation 2. Hypertension or pregnancy Hypertension and respective date of observation 3. Asthma and respective date of observation
	Infectious diseases	Malaria infection during the period of pregnancy or post partum Tuberculosis (TB): any form of tuberculosis prior to enrollment or any time after enrollment? Infections opportunists = Current opportunists infections that a mother has at enrollment or during the pregnancy period Does the patient have a history of Opportunistic Infections?	1. Any type of malaria and respective date of observation 2.Tuberculosis and respective date of observation 3.Current opportunistic infection and respective date of observation 4. History of opportunistic infection and respective date of observation.
	History of ARV side effects	patient shows side effects of treatment	1. Side effects = YES

3.7.Data analysis

Using the existing data under the IeDEA database, we have described socio demographic features, medical profiles and obstetric features of HIV-infected pregnant women newly on ART, We then determined the percentage of study participants with detectable VL at one point of check. Finally, we identified factors associated with a detectability of VL .

For data analysis, we used an IBM SPSS Statistics version 21 and described predictor variables using frequency and percentage and outcome of interest using a pie chart diagram.

To assess the association between predictor variables and outcome of interest we performed a bivariate analysis using chi squared test. Predictors were put together in multivariable analysis, and logistic regression model was performed to assess the association between variable of interest and explanatory variables .

3.8. Ethical Considerations

This study was nested from ER-RCBP activities which were ethically approved by Rwanda National Ethics Committee. A written approval from ER-RCBP to use their data was also provided. Provided data were de-identified to ensure a full protection of study participants.

Chapter four: Results

4.1. Characteristics of HIV infected pregnant women on ART

Table 3 shows that among 310 participants with available data at enrollment to HIV care program, almost 56% (n=155) had between 29-38 years old ,42 % (n=113) were married,66% (n=145) were primigravida, 56% (n=111) had 14-28 weeks of pregnancy, 61 % (n=181), were normal weight,75 % (n=9) were not having albumin in urine.

Among these new enrolled HIV infected pregnant women, 98% (n=305) had a viral load check post ART initiation. Of these, almost 82% (249) their viral load were <= to 20 copies/ml, 52% (n=100) had viral load check after 9 months post ART initiation and almost 83% (n=252) were in WHO HIV stage 1.

Concerning HIV disclosure, 61% (n =95) disclosed their HIV status compared to 35% (n=54) who did not.

Table3. Socio demographic and medical characteristics of HIV infected pregnant women on ART

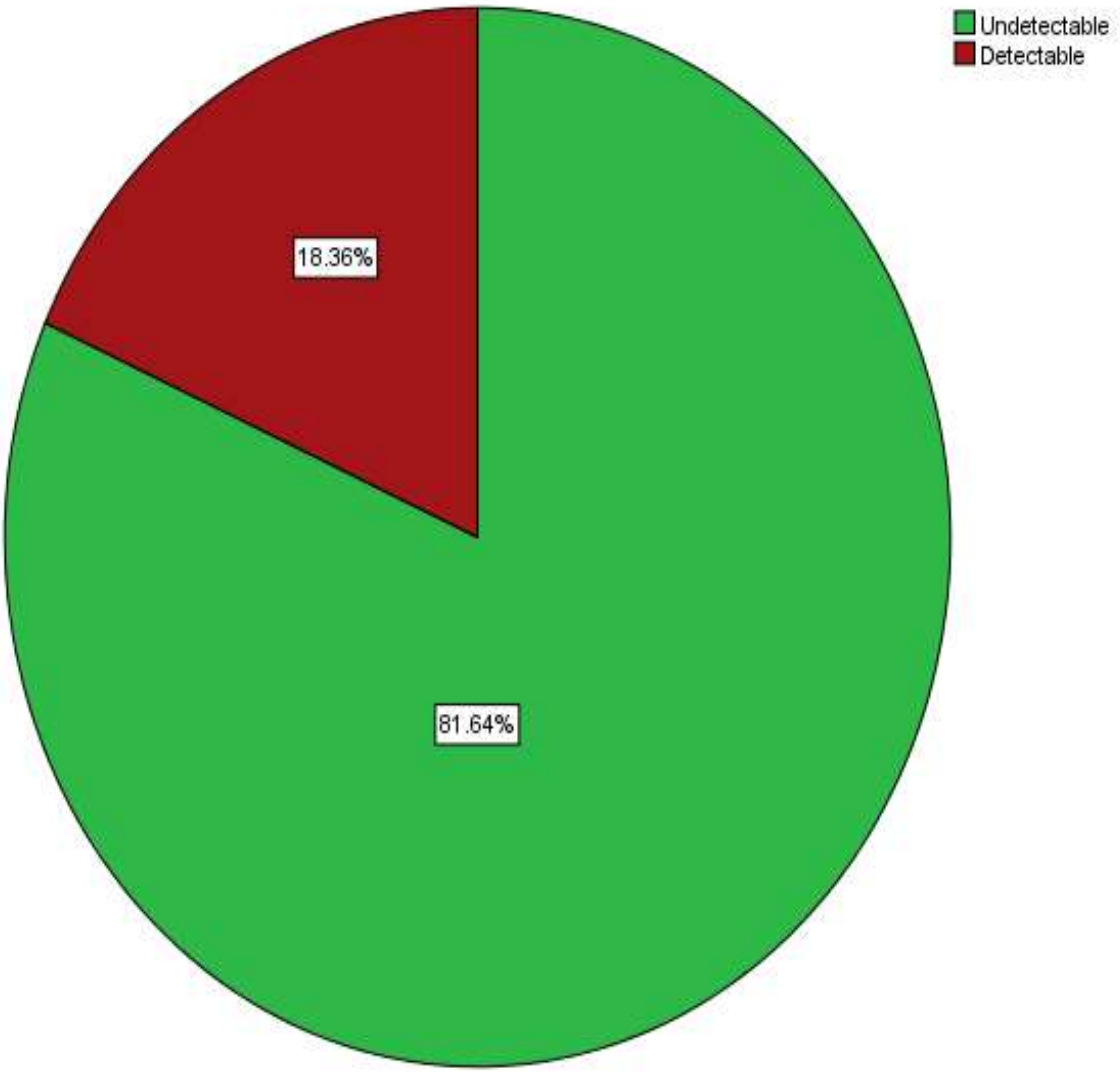
Variables	Frequency	Percentage
Age category (n=278)		
19-28 Years	96	34.5
29-38 Years	155	55.8
39-48 Years	27	9.7
Marital Status (n=272)		
Single	39	14.3
Married	113	41.5
Living with partner	76	27.9
Separated	19	7.0
Widowed	8	2.9
Never Married	2	.7
Unknown	15	5.5
Gestation age (n=198)		
< 14 weeks	49	24.7
14-28 weeks	111	56.1
> 28 weeks	38	19.2

Gravidity of Women (n=221)		
Primigravida	145	65.6
Multigravida	76	34.4
BMI Category (n=298)		
Underweight	29	9.7
Normal weight	181	60.7
Over weight	70	23.5
Obese	18	6.0
Urinary albumin (n=12)		
Negative	9	75.0
Trace/Positive	3	25.0
HIV Disclosure Status (n=156)		
Disclosed	95	60.9
Not disclosed	54	34.6
Unknown	7	4.5
Viral Load checks (n=310)		
Checked	305	98.4
Not Checked	5	1.6
Viral load category (n=305)		
< = 20 copies/ml	249	81.6
>20 -200 copies/ml	29	9.5
>200 - 1000 copies/ml	4	1.3
> 1000 copies/ml	23	7.5
Viral load Checks period post ART initiation (192)		
Less than 3 months	30	15.6
3 to > 6 months	34	17.7
6 to > 9 months	28	14.6
Over 9 months	100	52.1
WHO HIV_stage		
WHO stage 1	252	83.4
WHO stage 2	26	8.6
WHO stage 3	21	7.0
WHO stage 4	3	1.0

4.2. **Proportion of new enrolled HIV infected pregnant women with a detectable VL after six months post ART initiation**

Our outcome variable analysis indicates that almost 82 % (n=310) of the surveyed women had undetectable viral load compared to 18% with a detectable viral load. Refer to figure 1.

Figure1.Viral load detectability among new enrolled HIV infected pregnant women



4.3.1. Factors associated with detectable viral load at bivariate level

The following table 4 indicates that age category (P-value = 0.018) and viral load category (P-value 0.000) were found to be more likely associated with viral load detectability during pregnancy and postpartum. For the rest of variables there were no evidence for their likelihood association with the observed outcome.

Table 4.Bivariate analysis of viral load detectability among new enrolled HIV infected pregnant women

Variables	Viral load detectability		P-Value
	Undetectable	Detectable	
Age category			
19-28 Years	81	11	0.018*
29-38 Years	117	37	
39-48 Years	25	2	
Marital status			
Single	31	7	0.491
Married	93	19	
Living with partner	63	13	
Separated	13	6	
Widowed	6	2	
Never Married	1	1	
Unknown	14	1	
Gestation age			
< 14 weeks	38	10	0.452
14-28 weeks	94	16	
> 28 weeks	28	8	
Gravidity of Women			
Primigravida	116	26	0.856
Multigravida	60	15	
BMI Category			
Underweight	23	6	0.127
Normal weight	151	25	
Over weight	52	18	

Obese	13	5	
Urinary albumin			
Negative	6	3	1
Trace/Positive	2	1	
HIV Disclosure Status			
Disclosed	80	14	0.941
Not disclosed	44	9	
Unknown	6	1	
Viral load category			
< = 20 copies/ml	249	0	0.000*
>20 -200 copies/ml	0	29	
>200 - 1000 copies/ml	0	4	
> 1000 copies/ml	0	23	
Viral load Checks period post ART initiation			
Less than 3 months	23	7	0.643
3 to > 6 months	30	4	
6 to > 9 months	22	6	
Over 9 months	82	18	
WHO HIV_stage			
WHO stage 1	206	43	0.657
WHO stage 2	20	6	
WHO stage 3	15	5	
WHO stage 4	2	1	

4.3.2.Multivarible analysis results

The association between predicator and outcome variable was analyzed using multivariable regression model for binary outcome (full model) including all covariates considered for the study and a reduced model that only includes those variables which has a moderate trend toward significance that comprised Age category, marital status and HIV disclosure status.

Of these explanatory variables in table 5, none of them predict viral load detectability among new enrolled HIV infected pregnant or postpartum women.

Table 5. Multivariable analysis (Logistic regression for binary outcome)

Variable	Full model				Reduced model			
	P-value	OR	95% C.I.		P-value	OR	95% C.I.	
			Lower	Upper			Lower	Upper
Age Category								
19-28 Years	Ref							
29-38 years	.197	3.089	.557	17.127	.190	2.312	.661	8.084
39-48 Years	.999	.000	0.000		.998	.000	0.000	
Marital Status								
Single	Ref							
Married	.222	.191	.013	2.715	.350	.460	.090	2.343
Living with partner	.373	.295	.020	4.331	.534	.581	.105	3.211
Separated	.420	.179	.003	11.727	.694	.593	.044	8.022
Widowed	1.000	0.000	0.000		.999	0.186	0.000	
Unknown	1.000	.000	0.000		.999	.000	0.000	
Gestation age								
< 14 weeks	Ref							
14-28 weeks	.477	.515	.083	3.204				
> 28 weeks	.677	.626	.069	5.648				
Gravidity of women								
Primigravida	Ref							
Multigravida	.315	.318	.034	2.970				
BMI category								
Underweight	Ref							
Normal weight	.275	.124	.003	5.249				
Over weight	.437	.218	.005	10.168				
Obese	.473	.160	.001	23.703				
HIV Disclosure status								
Disclosed	Ref							
Not disclosed	.218	.177	.011	2.782	.115	.322	.079	1.319
Unknown	.999	.000	0.000		.777	.705	.063	7.928
WHO HIV stage								
WHO stage 1	Ref							
WHO stage 2	.236							
WHO stage 3	.089	10.034	.701	143.626				
WHO stage 4	.999	.000	0.000					

Source: Data analysis

Chapter five: Discussion

Our results showed that almost 98% (n=305) of new enrolled HIV-infected pregnant women had a viral load check post ART initiation ,most of participants were between 29-38 years old (56%) and married (42%). The same results were found in Kinshasa by Yotebieng M et al,2019 whereby of eligible women (n=1752) for his study, 1623 had a VL measured (92.63%),53% were aged between 25-34 years old and 68% were married(35).

HIV infected Women newly enrolled in HIV care with a detectable VL at one point of time of VL check post ART initiation while pregnant or postpartum were found to be 18.36 % (n=56) compared to 81.64% (n=254) with undetectable VL using a cut-off of <=20 copies/mL of plasma. Of these women with a detectable VL, 7.5% (n=23) had a VL > 1000 copies/ml of plasma. Surprisingly, this results are quite different from the findings of Kabeho study by Michelle M. Gill et al,2016 in Rwanda with the same VL detectability cut –off whereby only half of participant, 52.2% had undetectable viral load and 84.6% had <1,000 copies/ml (13). However, in Kinshasa,Yotebieng M et al,2019 used a VL cut off of <=40 copies/ml revealed that among eligible women,53% had undetectable VL Vs 47 % with detectable(35)

Conversely, these results were not far from the Rwanda target of VL suppression among general population on ART which is 90% in 2018(15) and almost the same to the findings of Teresa Bonyo et al,2015 in Zimbabwe with VL cut-off of <= 400 copies/ml whereby after 3 months post Art initiation almost 88% of HIV infected pregnant women achieved a VL suppression and 89% of breast feeding achieved a VL suppression(36). It is also quite different from what E C Joao et al,2012 found in Brezil with VL cut-off of < 1000 copies/ml whereby among the study participants, 65.4% archived a viral load suppression in the HAART group(37)

At bivariate analysis, age category (P value= 0.018) and VL value ranges (P value =<0.0001) were more likely to be associated with viral load detectability during pregnancy and postpartum period. Similarly, in Zimbabwe, Teresa Bonyo et al,2015 revealed that the risk of non-suppression among pregnant women was related to age (P value =0.001) less likely among those aged 15 – 25 years and those aged 25 – 35, compared to >35 years(36) .

At multivariable analysis, there was no much evidence that socio demographic features, nor medical features or obstetric factors that were associated with VL detectability during pregnancy or post-partum period. Similarly, Silveira Marysabel Pinto Telis et al,2002 in his study in Bresil revealed that there was no evidence that an individual clinical status would explain the undetectability of VL(38).

5.1. Study limitations

This study had a number of limitations; we think we omitted to look at pregnancy outcome which could have helped to explore the risk of having a detectable VL. Individual time for HIV test, ART initiation, VL test date was not coherent to some of variables and therefore we could not explore the time between VL test and ART initiation versus to pregnancy to all individuals.

5.2. Conclusion

Our findings indicates an overtime increase of VL measurement among HIV-infected pregnant or postpartum women which highlights the success of the Rwanda HIV treatment and prevention program

Nevertheless, MTCT remains a concern since 18.36 % had a detectable VL and of these 7.5 % failed to suppress their VL < 1000 copies/ml

Based on findings for this study, factor associated with VL detectability during pregnancy or postpartum period are highly needed to be more explored.

5.3. Recommendation

For HIV program in Rwanda,

Besides the observed success of the Rwanda HIV program in VL measurement, Viral load check timing and frequency in pregnancy need to be made shorter and defined for pregnant women to sustain the MTCT prevention

For the IeDEA network,

Collection and entry process of HIV routine data need to be strengthened and monitored.

Pregnancy and maternity information of HIV infected women need to be linked to their personal data into OpenMRS.

Overall,

Further studies are recommended to explore more factors that could be associated with VL detectability among HIV infected pregnant women newly enrolled to the program.

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Appendices

1. Request letter to use ER-RCBP IeDEA data

2. Approval letter to use program IeDEA data