

USE OF ANTIRRETROVIRALS IN THE GESTATIONAL PERIOD, THEIR IMPACTS AND THE PREVENTION OF VERTICAL TRANSMISSION OF HIV: SYSTEMATIC REVIEW

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Abstract: Introduction: Antiretroviral therapy (ART) is a right offered by the SUS to all HIV-positive pregnant women, making it efficient in preventing vertical transmission. **Objective:** search in the literature how the use of therapy can impact the health of the pregnant woman and her unborn child, what are the measures adopted in the country to prevent vertical transmission. **Methodology:** This is a descriptive study, with retrospective data collection, through a narrative review, through articles and publications found in the SCIELO, LILACS, PubMed, MEDLINE database, institutional publications from the Ministry of Health and articles from Brazilian Society of Infectious Diseases with a temporal scope from 2011 to 2021. **Final considerations:** It is well known that every drug, regardless of its origin, whether allopathic or herbal, brings adverse reactions to the body. Likewise, antiretrovirals prescribed for the therapy of HIV-positive women during pregnancy can cause undesirable reactions. However, the benefits of ART indisputably outweigh all the side effects arising from antiretrovirals and to date there is no other effective and safe way to prevent the transmission of HIV from mother to child.

Keywords: HIV-seropositive pregnant women, vertical transmission and antiretroviral therapy.

INTRODUCTION

AIDS (Acquired Immune Deficiency Syndrome) is one of the main public health problems and a priority epidemiological issue in Brazil and the world.¹ It was in the social context of the 1980s that AIDS infection emerged. The appearance of the infection and its initial trajectory were generally far from women, but they reached them in a short period of time.²

The first case definition of AIDS was published in the MMWR (Morbidity and

Mortality Weekly Report), in September 1982, based exclusively on the presence of opportunistic infections, when there was still no test available to identify the presence of HIV.³

The global AIDS epidemic had its first cases reported in the medical literature in early 1981, in the USA. More than three decades later, the number of HIV-infected patients worldwide exceeded 35 million in 2012.³ However, there are approximately 38 million (31.6 million to 44.5 million) people worldwide living with HIV by the end of 2019.⁴

Every pregnant woman must be tested for HIV at her first prenatal consultation. If the result is positive for HIV, the pregnant woman must be referred to prenatal care in specialized services for follow-up.⁵

The Combined Antiretroviral Therapy (ART) is indicated for all pregnant women infected with HIV, regardless of clinical and immunological criteria, and must not be suspended after delivery, regardless of the LT-CD4+ level at the time of starting treatment.⁶ The objective of ART is to keep the Viral Load undetectable throughout the gestational period.⁵

According to the Ministry of Health⁷, the use of ART in pregnant women and newborns is recommended, indication of cesarean section in women with unknown viral load (VL) or greater than 1,000 copies/mL after 34 weeks of gestation and non-breastfeeding, as strategies for reducing vertical transmission of HIV. Furthermore, pregnant women with CV-HIV less than 1,000 copies/mL, but detectable, can undergo vaginal birth, as long as there are no obstetric contraindications. Likewise, it is recommended that the parturient receive intravenous zidovudine (AZT).

For women who have HIV and plan a pregnancy, with medical guidance, who carry out interventions correctly during prenatal care, it is possible to have a birth with the risk

of vertical transmission of HIV reduced to less than 2%. However, without planning and follow-up, this risk can vary from 15% to 45%.⁸

Antiretroviral Therapy (ART) is a right, offered by the Brazilian Unified Health System, to all HIV-positive pregnant women. This guarantee proves to be efficient in terms of vertical transmission. Therefore, the interest in research occurred with the aim of searching in the literature how the use of therapy can impact the health of the pregnant woman and her unborn child, what are the measures adopted in the country to prevent vertical transmission and what is the best approach therapy and follow-up of these pregnant women.

In this sense, the present study aims to evaluate the impacts caused by the use of antiretrovirals in women during the gestational period, as well as the prevention of vertical transmission of HIV and to verify the effects generated in pregnant women who used antiretrovirals throughout the period. gestation and observe management and care during childbirth in order to avoid perinatal transmission, through a narrative review.

METHODOLOGY

This is a systematic review, built in accordance with PRISMA recommendations, on the use of antiretrovirals during pregnancy, their impacts and the prevention of vertical transmission of HIV.

Data were collected through the selection of scientific articles in journals indexed in the databases of the Scientific Electronic Library Online (SciELO), Latin American and Caribbean Literature in Health Sciences (LILACS), PubMed, the National Library of Medicine (MEDLINE) and institutional publications from the Ministry of Health and articles from the Brazilian Society of Infectious Diseases.

As eligibility criteria, national and

international scientific articles were included that are indexed on one of the platforms indicated above, in Portuguese or English, in addition to publications from the Ministry of Health; all works that comprise the terms of the keywords used; all articles and institutional documents, published between 2011 and 2021.

As a search strategy, all documents containing a combination of the following terms were considered: *HIV and pregnant women; vertical transmission; antiretrovirals and pregnancy.*

RESULTS

A total of 2,855 articles were retrieved, distributed on the SciELO – 445 platforms; LILACS – 563; PUBMED - 1,722 and MEDLINE – 125. Of these, 2,431 were excluded after selecting titles and abstracts. There was a total of 424 complete articles assessed for eligibility, 187 of which were excluded for being duplicated. 237 articles related to HIV and Pregnant Women were selected, of which 199 were excluded due to illegibility, ending with 38 complete works directly related to HIV, Pregnant Women and Vertical Transmission, which were synthesized and included in the systematic review (Figure 1).

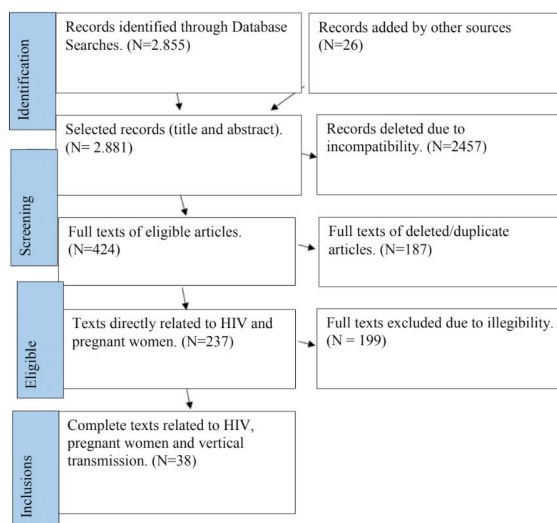


Figure 1: Flowchart of article selection (systematic review).

USE OF ANTIRETROVIRALS IN PREGNANT WOMEN

The diagnosis of the HIV virus in pregnant women poses several challenges for the health of the pregnant woman and her family, the most prominent being efforts to prevent mother-to-child transmission of the virus. And, adherence to antiretroviral therapy during pregnancy with the aim of reducing the viral load. The best option for treating pregnant women infected with HIV is the use of ART.³

People with HIV begin their treatments in the Unified Health System (SUS) through the Family Health Strategy Assistance (ESF) and this, in turn, coordinates all the care provided and the referral of the patient to a reference unit for comprehensive and resolute advice, monitoring and infection control.¹¹ HIV-positive pregnant women must be guided and referred to high-risk prenatal care or a Specialized Assistance Service (SAE) for monitoring throughout the prenatal period by an infectious disease specialist and obstetrician trained in HIV patients.¹²

Positive HIV diagnosis leads the team to discuss the use of antiretroviral therapy for the mother and, immediately at birth, for the child, planning a vaginal birth and/or cesarean section (if indicated) and advising not to breastfeed to reduce the risk TV (Vertical Transmission).¹³

In Brazil, antiretroviral therapy (ART) recommended by the Clinical Protocol and Therapeutic Guidelines for the Prevention of Vertical Transmission of HIV, Syphilis and Viral Hepatitis (PCDT/MS) is recommended for all pregnant women infected with HIV, free of clinical and immunological criteria, and not must be suspended after birth, regardless of the LT-CD4 level.¹²

Currently, six classes of antiretroviral drugs are available for the treatment of People Living with AIDS (PLWHA): Nucleoside and

nucleotide analogue reverse transcriptase inhibitors (NRTI/tNRTI); Non-nucleoside reverse transcriptase inhibitors (NRTIs); Protease inhibitors (PI); Integrase inhibitors (INI); Fusion inhibitors (IF) and CCR5 coreceptor inhibitors.^{3,14}

In the early 1990s, monotherapy with Zidovudine (AZT) was administered to prevent vertical transmission of HIV. However, the antiretroviral regimens currently used have evolved since the first successful trial using single-drug zidovudine prophylaxis in 1994.¹⁵

Although, nowadays, the scheme used is Combined Antiretroviral Therapy (CART). In Brazil, the initial regimen recommended by the Ministry of Health (MS) must preferably be the combination of two NRTI/NRTIs – Lamivudine (3TC) and Tenofovir (TDF) associated with the integrase inhibitor (INI) – dolutegravir (DTG). Furthermore, it is recommended whenever possible that zidovudine (AZT) must be part of any therapeutic combination. Exception to this scheme must be observed in cases of tuberculosis co-infection with HIV (TB-HIV), Women living with HIV (MVHIV) with the possibility of becoming pregnant and pregnant women.¹²

However, the Brazilian Ministry of Health recommends pre-treatment genotyping for all pregnant women infected with HIV, in order to guide the therapeutic regimen. It must also be considered a priority in the care network, since the choice of an effective antiretroviral regimen has a direct impact on HIV VT. Therefore, it is worth highlighting that the start of treatment must not be delayed by waiting for the results of this test.⁸

According to Fowler and employees,¹⁵ although there are benefits to combination antiretroviral therapy (ART) for mother and baby, they present risks; some studies have shown higher rates of adverse pregnancy

outcomes with maternal ART than with regimens containing fewer antiretroviral agents.

According to Friedrich,¹⁶ initiating early ARV therapy for all infected pregnant women has the potential to substantially improve maternal health and survival, in addition to making VT a rare event.

VERTICAL TRANSMISSION

Without treatment, HIV VT occurs in about 25% of cases. Approximately 75% of transmissions occur in the peripartum period and 25% in the intrauterine period. The risk is increased by 14 to 29% by breastfeeding.³

According to Kumar and employees¹⁷, vertical transmission of infectious agents from mother to fetus or newborn is a common mode of transmission of certain pathogens, and can occur through several different routes. HIV can be passed from the pregnant woman to the fetus through placenta-fetal transmission, during birth and postnatally during breastfeeding.¹⁸

HIV can be transmitted within the uterus by transplacental cellular transport, through a progressive infection of placental trophoblasts until the virus reaches the fetal circulation, or due to ruptures in the placental barrier followed by microtransfusions from mother to fetus.¹⁶

TRANSPLACENTAL TRANSMISSION

The developing fetus is supported by the placenta, which develops from fetal and maternal tissues. The placenta consists of a fetal portion, formed by the chorion, and a maternal portion, formed by the decidua basalis.¹⁹

The placenta and fetal membranes separate the fetus from the endometrium, the inner layer of the uterine wall. An exchange of substances, such as nutrients and oxygen, pass from maternal blood through the villus cell layers to fetal blood and metabolic

waste. Although the placenta is reasonably impermeable to microorganisms, several viruses and bacteria can cross it and infect the fetus. As the fetus does not have a functioning immune system and its protection is based exclusively on maternal antibodies, it is often unable to fight infections.^{20,21,22} It is the organ responsible for gestational success, however, its role in the vertical transmission of HIV-1 is still far from being completely understood.²²

According to Santiago,²³ human pregnancy is permeated by several adaptation mechanisms to avoid rejection of the fetus, which, as it is a semi-allogeneic tissue, must be rejected by the maternal immune system. The HLA-G molecule, present at the maternal-fetal interface, has an immunosuppressive characteristic. However, the role of HLA-G in the placenta is not fully elucidated, but it appears to act as a substitute for classical class I molecules, whose function is to inhibit immune responses against paternal MHC alleles presented by the fetus.²⁴

The analysis that the HLA-G gene has in relation to its expression in the regulatory processes of pregnancy is extremely important, since it is expressed during this phase of the female organism.²⁵

For Delves and employees,²⁴ the expression of HLA-G at the interface between placenta and maternal trophoblast appears to constitute a solution. The placenta expresses non-classical MHC class I proteins, HLA-G, HLA-E and HLA-F on trophoblasts, which may act to inhibit cytotoxicity by maternal NK cells, thus conferring protection.

The HLA-G molecule acts by inhibiting the cytotoxicity of Natural Killer (NK) cells and cytotoxic CD8+ T lymphocytes, providing a beneficial modulatory effect on pregnancy. Therefore, due to its immunosuppressive properties, this molecule may be involved in the persistence and progression of HIV-1 infection.²³ Furthermore, Kumar et al.

(2012) concluded that elevated cytokine and chemokine levels in placental plasma were associated with intrauterine rather than intrapartum MTF transmission. IP-10, which is both a T-cell chemokine and an enhancer of HIV replication. It is worth noting that studies of HIV-infected placentas indicate that it is mainly located in fetal placental antigen-presenting cells and in the syncytiotrophoblast.¹⁹

TRANSMISSION DURING BIRTH

It is the main form of VT, comprising around 65% of infections. This mode of transmission is caused by contact with infectious agents during passage through the birth canal, and refers to the exposure of the newborn's mucosa to maternal blood and other infected secretions during the baby's passage through the birth canal.^{17,26}

It is worth mentioning that all pregnant women must receive, on the day of delivery, AZT IV, loading dose and maintenance doses, according to the dosage schedule of injectable zidovudine. It must be started three hours before the beginning of the cesarean section, the period necessary to reach the adequate intracellular concentration of the medication and maintained until the umbilical cord is clamped.⁸

According to Salomão,²⁷ prolonged labor, rupture of amniotic membranes for more than 4 hours, viral load at birth, histological chorioamnionitis and prematurity are preponderant factors for VT. However, multivariate analysis with a model that included these factors showed that the most important predictor for VT is the viral load at the time of birth. In addition, other classically associated risk factors include: vaginosis, syphilis, use of illicit drugs, sexual intercourse without a condom, prematurity, low birth weight, invasive obstetric procedures and operative vaginal birth.²⁸

According to the protocol of the Ministry of Health (MS), seropositive pregnant women with an unknown viral load or greater than 1,000 copies/mL after 34 weeks of gestation, elective cesarean section is generally chosen in the 38th week of gestation due to the decrease the risk of vertical transmission of HIV.⁸ It is worth noting that elective cesarean section, in itself, reduces Maternal-Fetal Transmission (MFT) of HIV by 50% and, therefore, is indicated in all pregnant women who reach the peripartum period with detectable viral loads.²⁷

For pregnant women using antiretrovirals and with suppressed HIV viral load, if there is no indication for a cesarean section, a natural birth is indicated. Furthermore, in women with a viral load lower than 1,000 copies/mL, but detectable, vaginal delivery may be performed if there is no contraindication from the obstetrician.⁸

POSTPARTUM INFECTION THROUGH BREASTFEEDING

Breastfeeding increases the risk of mother-to-child transmission of HIV and must, therefore, be contraindicated in infected postpartum women.²⁷

Regarding breastfeeding, there is a 30-50% risk of VT with prolonged breastfeeding after the infant's first year of life. Feed newborns (NB) with milk formula until 6 months of age. Therefore, it is recommended by the Ministry of Health to indicate elective cesarean delivery, in specific situations, to suspend breastfeeding and ensure the necessary follow-up in postpartum care.^{8,29}

The HIV transmission through breastfeeding, proven by several studies, represents an additional public health problem for populations long affected by hunger. In Brazil, as in other countries around the world, breastfeeding has proven to be an important factor in HIV transmission.³

Mixed breastfeeding is also contraindicated. Pasteurized human milk from a milk bank accredited by the Ministry of Health (for example, pre-term or low birth weight newborns) can be used. If, at any point during follow-up, breastfeeding is identified, suspend breastfeeding and request a CV exam for the NB.⁶

According to Ribeiro-Fernandes,³¹ before the MS adopted prophylactic measures for vertical transmission, there was a major bioethical dilemma related to the treatment of pregnant women carrying the AIDS virus. The scarcity of publications made it difficult to choose a treatment capable of preventing vertical transmission to fetuses, without harm to the mother.

PATHOLOGICAL INVOLVEMENT AND BIOCHEMICAL SERUM CHANGES

To use ART during pregnancy is extremely important to avoid VT. However, there are many side effects observed in pregnant women such as: anemia, thrombocytopenia, allergy, changes in liver function tests, dyslipidemia and diabetes, but this is related to the use of ART.¹¹

However, antiretroviral medications, like all medications, are associated with side effects and toxicity. But the incidence of adverse reactions in pregnant women using ARV for HIV-VT prophylaxis is also low.^{8,32}

According to the Clinical Protocol and Guidelines for the Prevention of Vertical Transmission of HIV, Syphilis and Viral Hepatitis (PCDT), adverse effects are generally transient and of mild to moderate intensity, both in pregnant women and children.⁸

The Ministry of Health recommends that pregnant women starting treatment or after changing ART must have a new CV-HIV sample collected within two to four weeks. They must be evaluated regarding adherence

and drug interactions and the effectiveness of prescribed ARVs.⁸

The treatment regimen for Pregnant Women Living with HIV (GVHIV) recommended by the Ministry of Health when women with no history of prior exposure to ART, preferably to begin in the 1st trimester (up to 12 weeks of GA) is TDF/3TC/EFZ, if genotyping pre-treatment confirms the absence of mutations for ITRNN. Furthermore, if genotyping is not available or when transmitted resistance to NNRTI is demonstrated, start with TDF/3TC + ATV/r.³³

The TDF of the NRTI/tRNTI class can cause nausea, risks of renal toxicity, acute kidney injury and Fanconi syndrome. Therefore, this drug must not be used if there is previous kidney disease, glomerular filtration rate less than 60 mL/min or renal failure.^{8,34}

The 3TC, an NRTI/tRNTI, may present a flare-up of hepatitis in patients co-infected with HBV who discontinue the drug, pancreatitis, headache, dizziness, insomnia and peripheral neuropathy may occur.^{8,27,34}

According to Veronesi; Focaccia,³ the most common adverse events when using EFZ from the ITNN class; are: neurological disorders, sleep disorders, rash and teratogenicity.

Atazanavir/ritonavir (ATV/r) a Protease Inhibitor reinforced with ritonavir (IP/r) has the adverse effects of increasing bilirubin at the expense of indirect bilirubin with jaundice sometimes; nephrolithiasis and loss of kidney function (less common). Furthermore, its placental passage is approximately 10% and its fetal risk arises from the increase in bilirubin for newborns.^{27,35}

The preferred initial regimen for GVHIV from the 2nd trimester (from 13 weeks gestational age) TDF+ 3TC+ Dolutegravir (DTG). The antiretroviral DTG belonging to the INI class has adverse reactions such as insomnia, headache, nausea, vomiting, rash, rare reports of hypersensitivity reactions,

hepatotoxicity and increased transaminases in people co-infected with viral hepatitis.^{8,33,34}

The use of raltegravir (RAL), an INI, in the ARV regimen can be considered in pregnant women who start prenatal care or use ART late (end of the second trimester), and who have a contraindication to DTG. However, RAL is associated with nausea, headache, diarrhea, elevated CK, muscle weakness, and rhabdomyolysis. Case reports of increased transaminases in the third trimester of pregnancy.^{34,36}

Other antiretrovirals that are prescribed and/or recommended by the Ministry of Health as an alternative regimen are: Zidovudine (AZT), Abacavir (ABC), Nevirapine (NVP) and Darunavir/ritonavir (DRV/r).³⁶

AZT is an NRTI that can be used in cases of contraindication to TDF. Despite this, AZT is used in post-exposure prophylaxis. Its use may cause nausea, anorexia, headache, changes in taste, malaise, insomnia, anemia, neutropenia and fatigue as an adverse reaction.^{32,33} Prolonged use of AZT is associated with mitochondrial toxicity and peripheral lipoatrophy. As can occur with other medications in this class, there are reports of cases of lactic acidosis associated with the use of AZT.³⁷

ABC, another antiretroviral in the NRTI class, has the adverse effect of causing rashes and Stevens Johnson syndrome, especially in HLA-B 5701 positive carriers, which can be fatal.^{3,36}

NVP of the NNRTI class has the adverse reaction of rash (7%), generally maculopapular, of the erythema multiforme type; less than 1% progress to Stevens-Johnson Syndrome or epidermal necrolysis.³³

The antiretroviral DRV/r of the IP/r class may present the following adverse events: skin rash, hyperlipidemia, nausea, headache, hyperglycemia and occasional liver dysfunction at the beginning of

treatment.^{3,8,27,34}

Among the pathological conditions related to the use of ART in GVHIV, it is important to highlight lipodystrophy, or lipoatrophy, a syndrome characterized by the accumulation of fat in the dorsocervical region (“hump”), increased abdominal circumference and breast size, facial lipodystrophy, glutes and limbs, causing the prominence of the veins in the arms and legs. Glucose intolerance or gestational diabetes *mellitus* related to IP use and mitochondrial toxicity are also noteworthy.³

For Salomão,²⁷ side effects regarding the use of PIs are also relatively common changes in lipid metabolism, with an increase in cholesterol and triglycerides, and glucose, with glucose intolerance or, more rarely, even the development of diabetes.

According to Goldman; Ausiello,³² Morphological changes occur and can be quite distressing for patients, including lipoatrophy (loss of fat in the face and extremities) associated with zidovudine and lipoaccumulation associated with some PIs.

Veronesi; Focaccia,³ state that the risk of DM and insulin resistance is greater among those infected with HIV and using ART, compared to controls not infected with HIV.

DISCUSSION

ART is recommended for all pregnant women diagnosed with HIV, the Public Health System (SUS) together with SAE guarantees specialized attention, prescription and dispensing of Antiretrovirals (ARV). The use of ART is essential for the quality of life of GVHIV, as well as the health of the conceptus with regard to VT. HIV treatment with ART has dramatically improved clinical outcomes and patient life expectancy, making it one of the most significant examples of successful drug development in recent medical history.³

The Ministry of Health recommends

virial genotyping as pre-treatment for the appropriate initiation of therapy. However, treatment is started immediately, post diagnosis without genotyping results. The genotyping test must be requested immediately. After this procedure, ART must be introduced. However, the start of treatment cannot be delayed due to waiting for these tests. Performing genotyping for pregnant women must be considered a priority in the care network, since the choice of an effective antiretroviral regimen has a direct impact on HIV VT.^{33,35}

It is worth noting that the importance of genotyping suggests directing the choice of drug, in view of the fact that it allows detecting the occurrence of genotypic resistance of HIV-1 to antiretrovirals and selecting the most appropriate rescue therapy for patients treated by the SUS (Unified Health System).³

The AIDS infection is one of the most serious public health problems worldwide. Furthermore, HIV TV prevention is a major challenge for public health in Brazil, as factors such as: low education levels of pregnant women, social and economic barriers can interfere with adherence to the therapeutic regimen.³⁸ Therefore, Langendorf and employees,³⁹ conclude that the low level of education of WLHIV is closely related to low adherence to monitoring their clinical and obstetric condition, and also highlights the relevance of the qualification of professionals to carry out counseling and that it positively interferes with adherence to treatment, and is perceived by women as of extreme relevance.

In summary, pregnant women do not clearly understand AIDS, its forms of transmission, examinations and treatment, demonstrating the need to improve the health education process, in order to reduce the problems related to the disease during the gestational and parturition period.⁴⁰

Compliance with antiretroviral treatment

during pregnancy – which leads to a reduction in viral load – resulting in the greatest impact measure for the prevention of pediatric infection,⁴⁰. On the other hand, the management of CV-HIV prevention is influenced by socio-demographic factors that may or may not favor adherence to ART, adequate prophylaxis and monitoring of CV-HIV – protective factors for the child.^{8,38}

The VT can basically occur in three ways: intrauterine (transplacental), during childbirth and through breastfeeding. Transplacental contamination generates controversy among authors and publications. Yes, Delves and collaborators,²⁴ states that the HLA-G molecule, expressed between the placenta and maternal trophoblast, has an immunosuppressive characteristic that acts by inhibiting the cytotoxicity of NK cells (maternal) and cytotoxic T lymphocytes, providing a beneficial modulatory effect on pregnancy. However, due to its immunosuppressive properties, this molecule may be involved in the persistence and progression of HIV-1 infection.²³

However, SCHOENWOLF and collaborators,⁴¹states that HIV can sometimes cross the infected mother's placenta to infect the fetus. However, the mechanism by which the virus is able to breach the placental barrier and the consequences of placental viral infection are not completely elucidated.²² Therefore, according to Moore; Persaud; Torchia, 20 healthy individuals showing biallelic loss of HLA-G1 were identified, thus indicating that HLA-G is not essential for fetoplacental survival; human Extravillous Cytotrophoblast (EVT) cells are vulnerable to NK cell-mediated death; and the hypothesis does not explain why HLA-C, a polymorphic antigen, also expressed by EVT cells, does not evoke a local rejection response.

According to Ministry of Health,³⁶ vaginal delivery is always indicated, as long as pregnant

women have HIV-CV below 1,000 copies/mL, but detectable, and that they do not have any obstetric contraindications. In addition, episiotomy can be performed if necessary. Natural birth brings some advantages for both mother and baby, including faster recovery, absence of pain in the postpartum period, early discharge, lower risk of infection and hemorrhage.⁴²

The World Health Organization recommends the ideal cesarean rate between 10% and 15% and that cesarean birth is a surgical intervention, according to the standards of the Ministry of Health, and that, therefore, it can only be prescribed in situations in which normal birth is not possible. more than recommended.⁸

Therefore, it is important to highlight that during labor the conditions for the infusion of intravenous AZT need to be favorable at the time the parturient arrives at the specialized service already in labor, as recommended by the established protocol, in addition to maintaining the infusion until umbilical cord ligation.³³

It is worth mentioning that the current protocol does not concisely address what the procedure would be like for these parturient women in unfavorable conditions, already in labor.

ART is considered a milestone in the treatment for people with HIV, it markedly suppressed viral activity after its insertion, culminating in a reduction in morbidity and mortality among PLHIV, as well as an increase in quality and life expectancy. Although there are clear benefits of ART for mother and baby, they come with risks such as a variety of treatment-related metabolic abnormalities.³ However, the benefits always outweigh the potential adverse effects.¹⁵

According to Moura and his employees,¹¹ there are many side effects observed in pregnant women such as: anemia,

thrombocytopenia, allergies, changes in liver function tests, dyslipidemia and diabetes, but this is related to the use of ART.

Barros and his employees,⁴³ conclude that there is an association between the use of PI and inadequate carbohydrate metabolism. However, studies were inconclusive regarding the association between the use of PI during pregnancy and the development of gestational diabetes. Furthermore, if it is necessary to use PI in the treatment of pregnant women, more careful monitoring of blood glucose levels during pregnancy becomes plausible.

Regardless of the age group of carriers or pregnant women with the Moura virus,⁴⁴ concludes that the treatments used for the disease still have many side effects. Furthermore, when choosing the ideal ART for women, the compatibility of ARVs with contraception, pregnancy, presence of comorbidities and HIV prevention strategies must be considered, always individualizing each choice.⁴⁵

Among the relevant serum changes observed in GVHIV using PI is hyperlipidemia. The hypothesis is that PIs inhibit modified CRABP-1 and synthesis mediated by cytochrome P-450 (CYP), increasing the rate of apoptosis of adipocytes, reducing differentiation into pre-adipocytes and having the final effect of reducing adipocyte storage. triglycerides and greater release of lipids.³

According to Souza Neto and collaborators,⁴⁶ there was an increase in serum levels of Total Cholesterol (TC) and LDL-c throughout the first year after starting ART. Reinforcing the need to design monitoring and control strategies not only for HIV infection, but also for dyslipidemia and cardiovascular risk in these patients.

FINAL CONSIDERATIONS

It is well known that every drug, regardless of its origin, whether allopathic or herbal, brings adverse reactions to the body, a fact known since ancient times; Homer (in the Iliad) warned that mixing drugs could cause harm to health. Likewise, antiretrovirals prescribed for the therapy of HIV-positive women during pregnancy can cause undesirable reactions. However, the benefits of ART unquestionably outweigh all the side effects arising from antiretrovirals. It is worth noting that to date there is no other effective and safe way to prevent the transmission of HIV from mother to child.

It must also be noted that side effects related to the use of ART are rare, described in the

literature and only significantly observed in patients who use it for a long time and suffer from comorbidities such as Systemic Arterial Hypertension (SAH), obesity and those using PIs, which can progress to the emergence of heart and metabolic diseases.

It is evident that pregnant women using ART are mostly patients with low educational and socioeconomic levels; Therefore, it is imperative to provide care and reception to these patients in a different way, as ignorance of the severity of vertical transmission can contribute to non-acceptance and/or abandonment of therapy. Furthermore, it is necessary that all professionals involved in care (multidisciplinary team) have knowledge related to ART and VT to disseminate safe, comprehensive and consistent information.

REFERENCES

1. Lima ACMACC et al. Avaliação epidemiológica da prevenção da transmissão vertical do HIV. *Acta paul. Enferm, São Paulo*, v. 27, n. 4, p. 311-318, Aug. 2014.
2. Carvalho FT; Piccinini CA. Aspectos históricos do feminino e do maternal e a infecção pelo HIV em mulheres. *Ciênc. Saúde Coletiva* 2008; 13:1889-98;
3. Veronesi R; Focaccia R - **Tratado de Infectologia** – 5ª ed. vol 1. São Paulo: Atheneu, 2015;
4. UNAIDS, **Direitos Humanos, Saúde e HIV – World AIDS Day Report**. Global AIDS Update, 2020.
5. Martins-Costa, Sérgio et al. **Rotinas em Obstetrícia**. 7 eds. Porto Alegre: Artmed, 2017;
6. Fernandes CE; SÁ MFS. **Tratado de obstetrícia Febrasgo**. Rio de Janeiro: Elsevier, 2019.
7. BRASIL. Ministério da Saúde. Secretaria de Vigilância em Saúde. **Departamento de Doenças de Condições Crônicas e Infecções Sexualmente Transmissíveis. Protocolo Clínico e Diretrizes Terapêuticas para Prevenção da Transmissão Vertical de HIV, Sífilis e Hepatites Virais**. Brasília-DF; 2019.
8. BRASIL. Ministério da Saúde. Secretaria de Vigilância em Saúde. **Departamento de DST, AIDS e Hepatites Virais. Boletim Epidemiológico - AIDS e DST**. 2020;
9. Gil AC. **Como elaborar projetos de pesquisa**. 5. ed. São Paulo: Atlas, 2016;
10. Rudio FV. **Introdução ao projeto de pesquisa científica**. 42. ed. Petrópolis: Vozes, 2014. p. 71;
11. Moura SCC, Ferreira-Junior SRC; Matias MRSS et al. Adverse reactions to antiretrovirals presented by HIV patients: a scientific. **Research, Society and Development**, [S. l.], v. 10, n. 3, p. e50210313308, 2021.

12. BRASIL: Conselho Nacional de Saúde. **Recomendação nº038**, 23 de agosto de 2019. Dispõe que revogue integralmente a Lei nº 17.137, de 23 de agosto de 2019, que garante a parturiente a possibilidade de optar pelo parto cesariano, a partir da trigésima nona semana de gestação. Disponível em: <http://conselho.saude.gov.br/images/Reco038.pdf>
13. Goering RV et al. **Mims microbiologia médica e imunologia**. 6 ed. - Rio de Janeiro: Guanabara Koogan, 2020.
14. Tallo FS; Coelho OFL. **Tratado de medicina de urgência e emergência da graduação à pós-graduação**. Rio de Janeiro: Atheneu, 2018;
15. Fowler MD. Nursing's Code of Ethics, Social Ethics, and Social Policy. **Hastings Center Report**. Vol. 46, Issue S1 p. S9-S12, 2016.
16. Friedrich L, Menegotto M, Magdaleno AM, Silva CL. Transmissão vertical do HIV: uma revisão sobre o tema. **Bol Cient Pediatr**. 2016;05(3):81-6.
17. Kumar V; Abbas A.; Aster JC. **Robbins e Cotran – Patologia – Bases Patológicas das Doenças**. 9. ed. Rio de Janeiro: Elsevier, 2016;
18. Porth CM; Matfin G. **Fisiopatologia**. 9ª ed. Rio de Janeiro: Guanabara-Koogan, 2015;
19. Pawlina W; Ross MH. **Ross histologia texto e atlas: correlações com biologia celular e molecular**. Revisão técnica Telma Maria Tenório Zorn. 8. ed. Rio de Janeiro: Guanabara Koogan, 2021.
20. Moron AF; Camano L; JÚNIOR LK. **Obstetrícia**. Barueri, SP: Manole, 2011;
21. Schoenwolf GC et al. **Larsen embriologia humana**. Coordenação Cristiano Carvalho Coutinho; tradução Adriano Zuza, Alcir Fernandes. 5. ed. Rio de Janeiro: Elsevier, 2016;
22. Martinez J; Santiago MR.; Souza DA.; Silva GEB; Chahud F; Quintana SM; Mendes-Junior CT; Donadi EA; Fernandes APM. O papel da placenta na transmissão vertical do HIV-1. **Medicina (Ribeirão Preto)**, [S. l.], v. 49, n. 1, p. 80-85, 2016. DOI: 10.11606/issn.2176-7262.v49i1p80-85.
23. Santiago MR. Expressão das moléculas HLA-G em tecido placentário de mulheres infectadas ou não pelo HIV-1. 2014. Dissertação (Mestrado em Enfermagem Fundamental) - Escola de Enfermagem de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, 2014. doi:10.11606/D.22.2014.tde-22052014-160124.
24. Delves PJ et al. **Roitt fundamentos de imunologia**. Tradução Patricia LydieVoeux ; revisão técnica Arnaldo Feitosa Braga de Andrade. 13. ed. - Rio de Janeiro: Guanabara Koogan, 2018.
25. Barbosa SS; Da Silva LG; Dias De Souza PGV. Análise dos Polimorfismos Encontrados no Gene Hla-G com Quadros de Abortos Espontâneos Recorrentes, Utilizando Análise de Bioinformática; **Revista NBC - Belo Horizonte** – vol. 11, no 21, março de 2021.
26. Sripan P, Le Coeur S, Amzal B, Ingsrisawang L, Traisathit P, Huong NNG, et al. Modeling of In-Utero and Intra-Partum Transmissions to Evaluate the Efficacy of Interventions for the Prevention of Perinatal HIV. **PLoS ONE**. 2015;10(5):e0126647. doi:10.1371.
27. Salomão R. **Infectologia: Bases clínicas e tratamento / Reinaldo Salomão** - 1. ed. - Rio de Janeiro: Guanabara Koogan, 2017.
28. Zugaib M, Francisco RPV. **Zugaib obstetrícia**. 2020.
29. Nielsen-Saines K, Watts DH, Veloso VG, Bryson YJ, Joao EC, Pilotto JH, et al. Three postpartum antiretroviral regimens to prevent intrapartum HIV infection. **N Engl J Med**. 2012;366(25):2368-79. <https://doi.org/10.1056/NEJMoa1108275>;

30. Fernandes CE; SÁ MFS. **Tratado de obstetrícia Febrasgo**. Rio de Janeiro: Elsevier, 2019.
31. Ribeiro-Fernandes CC. Aspectos bioéticos na prevenção da transmissão vertical e manejo do tratamento com antirretrovirais em gestantes portadoras de AIDS no Brasil. **Resid Pediatr**. 2021;11(2):1-5 DOI: 10.25060/residpediatr-2021.v11n2-157
32. Goldman L, Ausiello D - **Cecil – Tratado de Medicina Interna**. Vol 2. 25ª ed. Rio de Janeiro: Elsevier, 2018;
33. CONITEC. Comissão Nacional de Incorporação de Tecnologias no SUS. **Relatório de recomendação. Protocolos Clínicos Diretrizes Terapêuticas. Prevenção da Transmissão Vertical do HIV, Sífilis e Hepatites Virais**. 2020. Disponível em:http://conitec.gov.br/images/Consultas/Relatorios/2020/20201125_Relatorio_PCDT-PTV_HIV_568_2020.pdf. Acesso em: 20 de out. 2021.
34. Jameson JL. et al. **Manual de medicina de Harrison**. 20. ed. Porto Alegre: AMGH, 2021;
35. Martins-Costa FM. **Condição Suspensiva: Função, Estrutura e Regime Jurídico**. ALMEDINA, 2017.
36. BRASIL. Ministério da Saúde. Secretaria de Vigilância em Saúde. **Departamento de Vigilância, Prevenção e Controle das Infecções Sexualmente Transmissíveis, do AIDS e das Hepatites Virais. Boletim Epidemiológico AIDS**. Brasília, DF; 2020;
37. Rachid M; SCHECHTER M. **Manual de AIDS**. 10ª ed. Rio de Janeiro: Revinter, 2017;
38. Galvão MTG, Cunha GHC, Freitas JG, Gir E, Reis RK. Condições sociodemográfica, materna e clínica de crianças expostas ao vírus da imunodeficiência humana. *Rev Rene*. 2014; 15 (1): 78-88.
39. Langendorf TF; Padoin SMM; Vieira LB; Mutti CF. Pregnant Women Who Have Hiv / Aids In The Context Of Vertical Transmission: Visibility Of National Scientific Production In Health. **Revista de Pesquisa Cuidado é Fundamental Online**, [S. l.], v. 3, n. 3, p. 2109–2125, 2011.
40. Ferreira C et al. Compreensão de gestantes HIV positivas sobre AIDS e transmissão vertical. *Revista Enferm. Foco*, 2020.
41. Schoenwolf GC et al. **Larsen embriologia humana**. Coordenação Cristiano Carvalho Coutinho; tradução Adriano Zuza, Alcir Fernandes. 5. ed. Rio de Janeiro: Elsevier, 2016.
42. Leguizamon Junior TL; Steffani JÁ; Bonamigo EL. Escolha da via de parto: expectativa de gestantes e obstetras. **Revista Bioética**. 2013, v. 21, n. 3, pp. 509-517. Disponível em: <>. Epub 13 Mar. 2014. ISSN 1983-8034.
43. Barros CA et al. Uso dos antirretrovirais na gestação e seus possíveis efeitos adversos. **FEMINA**, v. 39, n. 7, 2011. Disponível em:< <http://files.bvs.br/upload/S/0100-7254/2011/v39n7/a2695.pdf>>. Acesso em: 04 de out. 2021.
44. Moura SCC et al. “Reações adversas aos antirretrovirais apresentadas pelos portadores de HIV.” **Research, Society and Development** 10 (2021): n. pag.
45. Nóbrega IP; Manejo da terapia antirretroviral em mulheres. *The Brazilian Journal of Infectious Diseases - Educação Médica Continuada*. Vol 2 • No 5 • Outubro, 2016. Disponível em: <https://www.elsevier.es/pt-revista-the-brazilian-journal-infectious-diseases-269-articulo-manejo-da-terapia-antirretroviral-em-X2177511716600176>
46. Souza Neto AI et al. Dislipidemia e risco cardiovascular na terapia antirretroviral: o manejo dos fatores modificáveis. **Revista Brasileira de Cardiologia**, v. 26, p. 26-32, 2013. Disponível em: <<http://www.onlinejics.org/sumario/26/26-1/artigo2.asp>>. Acesso em: 04 de nov. 2021;