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Protocol for Diagnosis and Treatment of HIV in Pregnancy at a Hospital in the Brazilian Amazon

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Abstract— *Objective: to analyze HIV during pregnancy and develop a protocol for diagnosis and treatment of HIV during pregnancy to be used at the Hospital de Base Ary Pinheiro in the State of Rondônia, Western Amazon. Methods: bibliographic review from the database of virtual Scielo and Bireme. The following descriptors for research in the Portuguese language were combined: "HIV infections"; "Vertical transmission of infectious disease"; "Highly active antiretroviral therapy"; "Adverse effects" and "pregnancy". Results: as a result of the research, a protocol was developed to be followed by the professionals of the Obstetric Center of the Hospital de Base Dr. Ary Pinheiro (HBAP) in the management of HIV-positive patients during pregnancy. Final considerations: the most effective measure to avoid vertical transmission is the use of antiretrovirals and the use of combined antiretrovirals, in general, from the 14th week of gestation and the use of intravenous AZT at delivery. Adequate care for infected pregnant women involves, in addition to treatment with antiretrovirals capable of making and / or maintaining the viral load undetectable, general measures in prenatal care (such as care for the pregnant flora of the pregnant woman, vaccines), care during work delivery and suspension of breastfeeding. Thus, the expansion of the offer of antenatal care and the improvement of its quality are essential conditions for the reduction of vertical transmission to effectively occur.*

Keywords— ***HIV. Gestation. Protocol. Diagnosis and Treatment. Hospital.***

I. INTRODUCTION

Infection with the acquired immunodeficiency virus (HIV) is a worldwide pandemic and has assumed characteristics of feminization. Most infected women are of reproductive age. Mother-to-child transmission (vertical transmission - TV) is the primary means by which children acquire HIV infection worldwide. Infected children without treatment will die within two years.

In the absence of intervention, vertical transmission of HIV is around 25% (or up to 50% if we consider pregnant women with a clinical picture of AIDS). If the proposed guidelines are followed, these numbers may drop significantly (for example, the number of children infected

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by vertical transmission in the Southeast region of Brazil today is 4%).

Pregnancy is a very favorable moment for the diagnosis of the disease, due to the countless exams requested to pregnant women during prenatal care. Most infected pregnant women will be in the asymptomatic stage of the disease. Proper screening for HIV infection is of utmost importance, so that prophylactic measures are taken in time to obtain the best possible results. Two different types of HIV are known: 1 and 2. What predominates in the Americas is HIV-1, subtype B.

The Ministry of Health of Brazil made the notification of HIV-positive pregnant women and their children compulsory. The use of antiretrovirals is undoubtedly the attitude with the greatest impact in reducing vertical transmission. Studies are evolving, combined antiretroviral regimens are being recommended and more and more interventions are being proposed to reduce vertical transmission.

This research is a literature review on the diagnosis and treatment of HIV during pregnancy. We seek to have enough information to be able to diagnose and treat HIV in pregnancy, having the necessary theoretical foundations, to know the importance of HIV in pregnancy as obstetric morbidity, to identify risk factors for the development of the disease (mode of transmission, epidemiology, groups risk, therapy for the prevention of vertical transmission), make an early diagnosis, developing and indicating more appropriate measures to deal with HIV during pregnancy and, finally, as a general objective, develop a protocol for the diagnosis and conduct of HIV during pregnancy to be used at the Hospital de Base Ary Pinheiro in the State of Rondônia, Western Amazon.

II. METHODS

The methodological design followed a descriptive bibliographic review study, based on structured literature, obtained from books and scientific articles from conventional and virtual libraries. After defining the theme, a search for bibliographic review was carried out in the virtual databases of Scielo and Bireme. The following descriptors for research in the Portuguese language were combined: “HIV infections”; “Vertical transmission of infectious disease”; “Highly active antiretroviral therapy”; “Adverse effects” and “pregnancy”.

The bibliographical discussion focused on cross-cutting themes such as the conceptual basis of HIV, types of HIV and epidemiology, clinical manifestations, vertical transmission, use of illicit drugs, unprotected sexual practices, maternal factors, obstetric factors, prolonged labor, fetal factors, attached factors, viral factors, serological screening and diagnosis, concern and precaution of the medical team, treatment, adverse effects of antiretrovirals during pregnancy, general adverse effects, among other variables.

The protocol for the diagnosis and management of HIV patients during pregnancy for the Obstetric Center of Hospital de Base Dr. Ary Pinheiro is based on the literature review and medical experiences and is structured in the sequence of the description of the infection with the indicative conditions of immunodeficiency, prenatal serological diagnosis, prenatal exams, prenatal and postpartum care, drug treatment during pregnancy, prophylactic regimen using AZT at the time of delivery, care and assistance during delivery.

To carry out the protocol, the researchers asked the Ethics Committee for Research in Human Beings - CEP of the Hospital de Base Ary Pinheiro, waiving the Informed Consent Term because the study did not require intervention in the patient or collection of biological material, and no possibility of embarrassment to the patient and family.

III. LITERATURE REVIEW

Infection with the acquired immunodeficiency virus (HIV) is a worldwide pandemic, affecting almost 40 million people worldwide and more than 700.000 in Brazil, considering that these numbers may be underestimated by more than 20%. At the beginning of the epidemic, in the 1980s, most new cases of infection occurred in men with homosexual behavior. The epidemic evolved and took on a characteristic of feminization and, in the group of adolescents, there is already a trend towards a greater number of infected girls than infected boys. It is estimated that more than 200.000 women in Brazil have the human immunodeficiency virus, with a prevalence of pregnant women affected around 0.4% [1].

Mother-to-child transmission (vertical transmission) is the main means by which children acquire HIV infection worldwide [2].

According to Freitas et al [3]:

> It is known that approximately 68% of HIV-positive women are of reproductive age, and more than 90% of children infected with HIV have been infected due

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> to vertical transmission. Most women become infected through heterosexual transmission.

Santos et al [4] claim that:

> The AIDS epidemic in the world has been the subject of numerous studies and research that seek not only to reduce transmission and mortality, but also to improve the quality of life of individuals living with HIV.

According to Zugaib [5]:

> The importance of studying HIV in pregnancy lies in the effort to reduce the rates of vertical transmission of the disease. The incidence of human immunodeficiency syndrome acquired in children has been decreasing and a series of studies in the medical literature worldwide shows a significant reduction in vertical transmission rates.

In the absence of intervention, vertical transmission of HIV is around 25%. It is estimated that in symptomatic pregnant women with a clinical picture of AIDS, these rates are around 50%. The reduction to levels between zero and 2% is already a reality in developed countries. In the Southeast region of Brazil, the number of infected children is currently below 4% [5].

Intrauterine transmission is less frequent in the first trimester. Most cases of vertical transmission happen near or during delivery. Breastfeeding represents an additional risk of transmission that can vary from 7% to 22%. This risk increases to approximately 30% when the mother's infection occurs during the breastfeeding period [3].

For Zugaib [5], the control of vertical transmission is related to the quality of prenatal care, peripartum antiretroviral prophylaxis and the suspension of breastfeeding.

In prenatal care, it is extremely important to adequately screen for HIV infection, so that prophylactic measures are taken in time to obtain the best possible results. The use of combined antiretroviral therapy in HIV-positive pregnant women and the maintenance of viral load below 1.000 copies \ ml not only prevent vertical transmission, but also prevent the appearance of opportunistic infections, which can lead to obstetric complications, such as prematurity. The administration of zidovudine (AZT) in the peripartum period is the attitude of greatest impact in reducing vertical transmission of HIV. Elective cesarean section and suspension of breastfeeding corroborate the decrease in these rates.

The transmission of the virus through breastfeeding reaches 42%, as observed in African countries, where the few resources do not allow the reduction of vertical transmission to desirable levels [5].

The period corresponding to five years showed a tenfold increase in coverage of antiretroviral treatment in the world, reaching almost three million people. Antiretroviral coverage in HIV-positive pregnant women, for the prevention of vertical HIV transmission, increased from 9% to 33%. The rapid expansion of treatment has guaranteed a decline in the annual number of AIDS deaths since 2005 (2.3 million), including deaths of individuals under the age of 15. It should be noted that children infected by vertical transmission without treatment will die in about 2 years [1].

According to the Febrasgo High Risk Gestation Manual [1]:

> Studies carried out in several countries show that the rate of vertical transmission ranged from 5 to 35%, with the highest rates in developing countries. However, there has been a significant decline in this rate over time, as a result of the introduction and expansion of specific therapeutic approaches for HIV-positive pregnant women in different areas of the world. In developed countries, interventions such as the use of antiretroviral therapy, elective cesarean section and artificial breastfeeding resulted in a reduction in the TV rate from 15.5% before 1994 to 5.1%, between 1997 and 1998, and to 0.99%, between 2001 and 2002, when potent antiretroviral therapy (ART) became widely used.

According to the Treatment Guide - Recommendations for Prophylaxis of Vertical HIV Transmission and Antiretroviral Therapy in Pregnant Women of the Ministry of Health [6]:

> In a national, multicentre study, a reduction in the vertical transmission rate from 8.6% to 3.7%, over a 3-year period in the Southeast region of Brazil, was demonstrated.

An important marker for the adequate application of HIV TV prophylaxis actions is the use of injectable AZT in parturient women. This indicator has remained stable over

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the past 3 years - around 57%. Such data seems to point to the need to expand the use of rapid tests in maternity hospitals and during prenatal care, primarily in situations where the diagnosis of HIV infection cannot be made in a timely manner for the adoption of measures that aim to the reduction of HIV TV [6].

This suggests that the main factors that hinder the decrease in national rates of vertical transmission of HIV are the late diagnosis of HIV infection during pregnancy, the low adherence to technical recommendations by health services (such as those that do not offer serology) for HIV during prenatal care at recommended times) and the quality of care, especially in regions with less service coverage and less access to the health network.

Freitas et al [3] claim that:

> The World Health Organization proposes four strategic points to try to reduce the number of HIV-infected children: primary HIV prevention in women of reproductive age; guidance on contraceptive methods for HIV-positive women; prevention of vertical transmission; and treatment for women and their families.

In order to make everyone aware of the importance of requesting HIV serological testing in pregnant women, the Ministry of Health has made the notification of HIV-positive pregnant women and their children compulsory. Many advances have been made allowing for a better understanding of the pathogenesis and treatment of HIV infection. Combined regimens that maximize suppression of viral replication are now recommended. Although special considerations must be made in relation to pregnancy, with possible adverse effects on the fetus and the newborn, this does not invalidate the choice of antiretroviral treatment based on the standard recommended for other adults, in order to further reduce the risk of vertical transmission [3].

In the historical process of the pathology, the acquired immunodeficiency syndrome (AIDS) was first described in 1981, when it was found that a group of patients had cellular immunity disorder and *Pneumocytis carinni pneumonia*.

The Febrasgo High Risk Gestation Manual [1] states:

> HIV infection was initially described in 1982, as a new clinical syndrome among individuals with homosexual practice, characterized by the appearance of opportunistic infections, associated with important immunity impairment.

Two different types of HIV are known: 1 and 2. HIV-2 is found predominantly in West Africa, can be transmitted from mother to child, but has a slower and less severe clinical course of infection. For HIV-1, numerous subtypes are recognized. Subtype B predominates in the Americas (including Brazil) and Europe; types A, C and D in Africa and E is found in Asia. Subtype C seems to be related to higher plasma viral load (CV) and vaginal elimination, when compared to subtypes A and D [1]. The etiologic agents of the immunodeficiency syndrome are human immunodeficiency viruses. HIV - 1 and HIV - 2. Most cases in the world are caused by HIV - 1; HIV - 2 infection is endemic in West Africa.

Differences in vertical transmission (VT) are also associated with specific viral subtype behaviors, in addition to immune responses and the ability to recognize viral antigens by the host and the effect of preventive interventions [1].

Konopka et al [7] analyzed the clinical and epidemiological profile of HIV-infected pregnant women attended in the prenatal care at the Hospital Universitário de Santa Maria (RS) and concluded:

> Young women in vulnerable socioeconomic situations, with low schooling and multiparous women constitute the majority of the population of HIV-positive pregnant women attended at the service.

When it comes to pathophysiology, HIV has tropism for lymphocytes, macrophages and dendritic cells (Langhans). These cells have in common a membrane receptor called CD4. This is the virus receptor. However, for cellular penetration of the viral genome to occur after binding of the virus to CD4, at least two co-receptors, called CCR5 and CXCR4, are required. Without them, it is not possible to proceed with the viral reproductive cycle. As soon as the viral RNA gains the host cell cytoplasm (in this case, the CD4 + T lymphocyte), it undergoes the action of reverse transcriptase, an enzyme capable of transcribing a double helix DNA from a single helix RNA. Now, the viral genome has become DNA and can then integrate with the DNA of the cell's nucleus. Once integrated, using the host's enzymatic arsenal, the virus's genetic code manages to produce its own proteins and a reliable copy of its RNA which, when joined together, have just formed a "child virus". During viral replication, thousands of "child viruses" sprout from the host cell, taking advantage of the material in its plasma

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membrane to form its "envelope" - the lipoprotein envelope of the virus. When it replicates on a large scale, it harms cell physiology, culminating in its death [8].

After infection, over time the number of T cells decreases insidiously and progressively, ultimately resulting in profound immunosuppression. Thus, the common denominator of AIDS is profound immunosuppression, mainly of cellular immunity, which causes several opportunistic infections and neoplasms. Infected monocytes, and infection of microglia brain cells can cause neuropsychiatric abnormalities. HIV-infected people also have a higher incidence of cancer, notably kaposi sarcoma, B-cell and non-Hogdkin lymphomas, as well as some carcinomas.

It is speculated that whatever the antiretroviral drug, the phenomenon of emergence of resistant viral "quasi-species" is intrinsic and inevitable in the medium or long term, depending on three main factors: mutation rate (lower in DNA viruses and higher in the case of RNA), replication rate and selective pressure exerted by the drug (function, basically, of its potency, concentration and duration of exposure). In the case of HIV, the viral turnover is in the range of 1,010 viral particles per day, meaning that 99% of the virions produced at each instant are from infected cells in the last 2 weeks; thus, knowing that reverse transcriptase makes an average of one error per genome per duplication cycle, it is concluded that the mutability rate is quite high [1].

At least a decade ago, it was believed that the relative immunodeficiency of pregnancy contributed to the progression of the disease. Currently, it is known that changes in CD4 and CD8 lymphocyte counts and proportions occur during pregnancy with a physiological and adaptive character of the pregnant woman's body, with no significant differences between HIV-positive and HIV-negative pregnant women [5].

In HIV infection in non-pregnant adults, indications for antiretroviral therapy follow well-established standards, which are not compatible for use in pregnant women. The indication for antiretroviral therapy in pregnant women is much broader, focusing on the prophylaxis of vertical transmission of the disease. For this reason, the more widespread use of antiretrovirals raises concerns about the risk of virus resistance and disease rebound. Recent studies note that, despite the increase in viral load in the puerperal period, there was no evidence of increased rates of infection progression to AIDS, showing a fundamental role of the adaptive immunological mechanisms of pregnancy [5].

What is known about clinical manifestations. The exact incubation period from infection to clinical disease is unknown, however, it is usually 2 to 3 months.

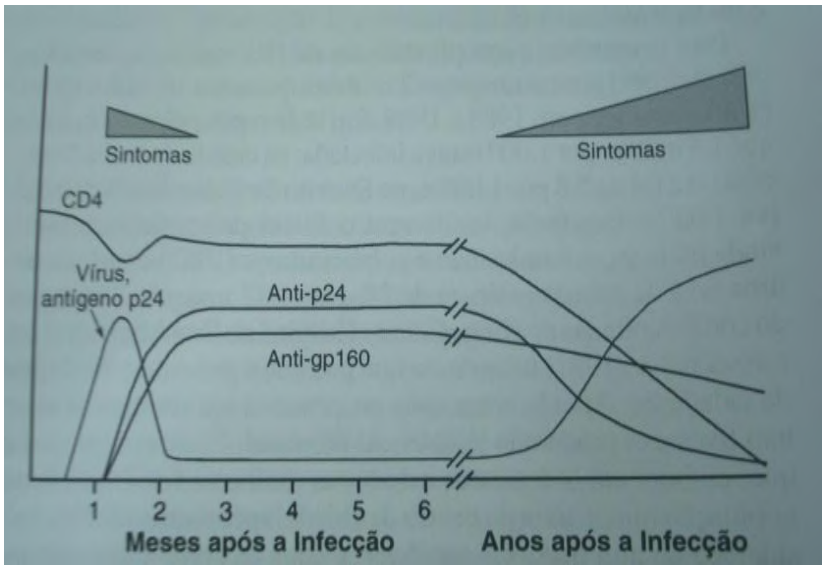

Fig.1: Schematic model of the natural history of HIV-1 infection

HIV-1 infection runs with a wide spectrum of clinical presentations, from the acute phase (which can be asymptomatic or manifest as an acute retroviral syndrome) to the advanced stage of the disease, with the defining manifestations of acquired immunodeficiency syndrome (AIDS) . In untreated individuals, the average time between infection and the onset of the disease is estimated at 10 years [1].

Acute retroviral syndrome resembles infectious mononucleosis and is associated with elevated plasma

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viremia and a transient but significant drop in CD4 lymphocyte count. Symptoms include high fever, sweating, transient lymphadenomegaly, with symmetrical, mobile and painless nodules, mainly affecting the anterior and posterior cervical, submandibular, occipital and axillary chains, with progressive decrease in the first weeks. Splenomegaly, fatigue, loss of appetite, depression, oral and genital ulcers can also occur, sometimes reaching up to the esophagus. Some patients may develop a rash after the onset of fever. The clinical diagnosis, in this phase, usually goes unnoticed by the transitory character of the symptoms [1].

With the exception of lymphadenopathy, in the clinical latency phase there are no changes on physical examination. Laboratory changes may occur, with mild thrombocytopenia being the most frequent. Some individuals may have mild anemia and leukopenia. Nonspecific skin lesions can also occur as seborrheic dermatitis, folliculitis and molluscum. As long as the CD4 lymphocyte level is above 350, the most frequent infectious episodes will be bacterial. As the disease progresses, atypical presentations of infections, late response to antibiotic therapy and / or reactivation of old infections such as tuberculosis and neurotoxoplasmosis begin to be observed [1]. The appearance of opportunistic infections and neoplasms is defining AIDS. AIDS-indicating diseases include multiple opportunistic infections, such as esophageal or pulmonary candidiasis, herpes simplex and persistent, tuberculosis, cytomegalovirus, Pneumocystis, toxoplasmosis, cervical cancer and others.

Most HIV-infected pregnant women present in the asymptomatic stage of the infection, so the clinical examination adds little in this regard. In the acute phase of the infection, or when the pregnant woman shows signs of immunodeficiency, the diagnosis can be made; however, confirmed only with serological tests [4].

Recently, a CD4 + count below 200 / ul is also considered definitive for the diagnosis of AIDS in HIV positive individuals. The AIDS mortality rate is extremely high, with many patients dying within 2 years.

It is important that health professionals should ensure that all pregnant women are advised and encouraged to be tested for HIV infection in order to allow women to know their infection status both for their own health and to reduce the risk of perinatal transmission of HIV. There are a number of factors that increase the risk of mother-to-child transmission of HIV, which is why they need early identification, which allows for appropriate intervention, whenever possible [4]. The use of illicit drugs causes placental vascular damage, increasing the permeability of the placenta, and, consequently, the risk of passing HIV and intrauterine transmission. In pregnant women who use illicit drugs, antiretroviral therapy, even if prophylactic, should be started as early as possible [4]. Unprotected sexual practice increases the risk of reinfection by HIV itself (causing an increase in viral load), in addition to exposure to resistant variants of the virus and the acquisition of other STDs [6] and the multiplicity of partners [4]. Important maternal factors are the high maternal viral load (CV): from a practical point of view, vertical transmission occurs in pregnant women with a CV> 1,000 copies \ ml (transmission with a CV below this number is considered a rare event). Low T-CD4 lymphocyte count: in general, the reduction in T-CD4 lymphocytes is related to high viral load. Reduction of neutralizing antibodies. Acute infection during pregnancy: in this situation, transmission occurs more than 50% of the time. Associated infections: genital and systemic infections increase vertical transmission. Smoking: Cigarette causes placental lesions that allow the virus to pass through this organ. Non-use (prophylactic or therapeutic) of antiretrovirals (ARV). The use of antiretroviral therapy (ART) is one of the most effective actions for reducing VT, which has been demonstrated in several studies (level of evidence 1a, degree of recommendation A) [4].

Obstetric factors are the prolonged rupture of the membranes [4]. According to the Ministry of Health Manual [6], the longer the rupture time, the greater the risk of HIV transmission, particularly when longer than 4 hours.

Regarding prolonged labor, it is important to observe the exposure to maternal blood: decreasing the newborn's contact with maternal blood reduces the chance of VT (episiotomy should be avoided, rapid clamping of the umbilical cord, newborn as soon as possible); Invasive fetal propaedeutics: invasive procedures increase the risk of VT (cordocentesis, amniocentesis, among others) [4]. According to the Ministry of Health Manual [6] this is due to placental injury. Observe the type of delivery. Several studies show that elective cesarean section reduces the chances of HIV VT in women with CV> 1,000 copies \ ml (there is no evidence of benefits of elective cesarean section in women with CV below this level). Vaginal delivery (especially with episiotomy or using forceps) presents a higher risk of VT even when compared to emergency cesarean sections in women with CV> 1,000 copies \ ml (level of evidence 1st degree of recommendation A) [4].

The Ministry of Health Manual [6] explains:

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> The presence of uterine contractility triggers placental microtransfusions, leading to greater contact of the fetus with maternal blood.

Regarding gestational age, the Ministry of Health Manual [6] clarifies that the TV rate is inversely proportional to gestational age, that is, every effort must be made to ensure a good quality of prenatal care, in order to avoid preterm labor [4]. The transmission of HIV through the uterus is greater in the third trimester of pregnancy, which justifies that all pregnant women are under treatment during this period.

Fetal, adnexal and viral factors must be observed in detail. In fetal factors, genetic susceptibility: fetuses and newborns that express secondary HIV receptors (especially CCR-5, CXCR-4); Reduced function of fetal cytotoxic lymphocytes; Failure in the integrity of the skin and mucous membranes; Prematurity and low birth weight. In the adnexal factors. Expression of HIV receptors in the placenta: the expression of CD4, CXCR-4 and CCR-5 receptors in the placenta increases the risk of infection of this tissue and, consequently, vertical transmission; Impairment of the integrity of the placenta: adnexal infections (placenta and membranes), trauma and solutions of continuity of the placental surface resulting from infections and smoking [4]. Viral factors. Viral genotype and phenotype: subtypes D and E of HIV 1 are more virulent and more transmissible than the others; Resistance to ARVs; Greater macrophage tropism; Postnatal factors; Breastfeeding (there is an additional risk with each feeding, which varies from 7 to 22%) [4]. In cases of acute maternal infection, breastfeeding increases HIV VT to 29% [6]. It has been proven that mother-to-child transmission is responsible for most human HIV infections among children.

The Febrasgo High Risk Pregnancy Manual, reports a study by Magder and colleagues in 2005, which showed that low birth weight was strongly associated with intrauterine TV, while gestational age at birth, CD4 before delivery, year and weight at birth and duration of membrane rupture greater than 4 hours were associated with intrapartum VT. This study reiterated that there was greater control of peripartum risk factors and consequent deviation to increase intrauterine transmission in the absence of antiretroviral therapy.

The Ministry of Health [6] considers that high viral load is the main risk factor associated with vertical transmission of HIV. If there is an imperative need for single invasion, such as drainage of polyhydramnios, the use of 2 mg / kg of maternal weight of intravenous AZT before puncture can reduce the risk of VT of the virus in question. For the diagnosis of fetal anemia in Rh isoimmunization, amniocentesis can be replaced by assessing the systolic peak velocity of the fetal middle cerebral artery (doplervelocimetry). It is clear, however, that these behaviors must be thoroughly discussed with family members [9]. It is known that the umbilical cord blood test is not suitable for diagnosing intrauterine HIV-1 infection, and does not offer the necessary sensitivity or specificity for this diagnosis. Due to all these difficulties and limitations, the diagnosis of fetal HIV-1 infection, without risks to the fetus, is not yet possible [9].

Serological screening and diagnosis of HIV infection. Knowledge of the serological status of HIV infection and the early diagnosis make it possible to adopt measures that substantially reduce the risk of vertical HIV transmission [6].

Testing and counseling are essential and are part of prenatal care, as recommended by the Ministry of Health, which recommends testing in the first trimester or the first prenatal consultation, repeating it in the third trimester. The physician must perform pre- and post-test counseling and request an anti-HIV test during prenatal care, safeguarding confidentiality and recording in the medical record that such measures were adopted, as well as the consent or refusal of the pregnant woman to perform the exam [6]. It is important to emphasize that the test must be offered and its performance is voluntary, confidential and confidential, for the pregnant woman and her partner (s).

Curitiba, capital of the State of Paraná, was the first among Brazilian capitals to implement decentralized HIV serological testing for all pregnant women monitored by SUS [10].

When a seropositive pregnant woman is discovered, it is imperative that the serological examination of her sexual partner be performed, which makes pregnancy a window of opportunity for the diagnosis of the couple's viral infection.

According to studies carried out by Feldmann et al [11], following articles and resolutions of the Code of Medical Ethics, on HIV positive pregnant women who omit their sexual partner from being a carrier of the virus, the best approach adopted is as follows:

> The doctor must convince the pregnant woman to reveal her condition of being HIV positive to her sexual partner. If the patient is resistant to unveiling the status, the doctor has the duty to intervene and inform the partner, for his protection. Breach of confidentiality, in this case, is

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> done for just cause, which exempts the doctor from problems or legal implications.

Screening for HIV infection during pregnancy should be performed using a test capable of detecting anti-HIV 1 and anti-HIV 2 antibodies. This first serological screening step, called step I, when it results in a non-reactive test, determines in blood sample as a negative HIV sample. In these cases, post-test counseling is advised, warning the pregnant woman about risk situations [5].

Commercial kits for detecting HIV infection have undergone considerable changes, allowing to reduce the period of immunological window and increasing the capacity to detect HIV-1 and HIV-2, in addition to several subtypes [6]. According to the Ministry of Health [6], the use of the following laboratory methods in the test of step I is allowed: Immunoenzymatic assay - ELISA; Immunoenzymatic assay of microparticles - MEIA; Immunological assay with chemiluminescent staining and derivations - EQL; Enzyme-linked fluorescent immunological assay - ELFA; Magnetic chemiluminescent immunological assay - CMIA; Rapid tests: immunochromatography, agglutination of particles in latex or immunoconcentration; New methodologies registered with ANVISA and validated by the Department of Surveillance, Prevention and Control of Sexually Transmitted Diseases and Acquired Immunodeficiency Syndrome.

Once the test shows a positive result, another test must be performed on the same sample. This second stage, called stage II or of serological confirmation, presupposes the use of another type of test, whose methodological principle or investigated antigens must be different. If the step II test is positive, the patient's first blood sample is considered to be positive for HIV, and another sample should be collected immediately and repeat step I in this new sample. The finding, in the second sample, only of the positive step I already allows to issue a final definitive report that the blood sample is positive for the HIV virus [5].

Santos et al [4] propose another way to conduct positive tests in step I:

> If the result is positive, the serology must be repeated in a second collection. Continuing the ELISA positivity, it is necessary to carry out a confirmatory test, which has greater specificity (indirect immunoflorescence or Western-blot).

If still in the first sample, after positive step I, the test in step II is negative or indeterminate, the second sample should not be taken immediately, but after a period of 30 days, to avoid repeating the exam in the period of the so-called “window immunological ”. In this situation, the second sample is submitted to both stage I and stage II [5].

According to the Ministry of Health Manual [6], the methods used in the step II test are as follows: indirect immunofluorescence - IFI; Immunoblot - IB; Immunoblotrápido - IBR; Western Blot - WB; Other methodologies registered with ANVISA and validated by the Department of Surveillance, Prevention and Control of Sexually Transmitted Diseases and Acquired Immunodeficiency Syndrome.

For the interpretation of the results and release of the report, the results obtained in the tests of Steps I and II are analyzed together.

When the step I test of the first sample is inconclusive, step II is not performed on this blood sample. In this case, the second sample is taken immediately and step I is repeated. Resulting negative, the patient receives the final definitive diagnosis of a negative sample for HIV. As a result of the test of step I of this second sample, again inconclusive, the final result will be of an undetermined sample for HIV, and the patient must repeat the serology after 30 days, to rule out that the inconclusiveness is due to the “immunological window”. Finally, if in the second sample the triaging test of step I is positive, then the confirmatory test of step II will be carried out on that sample, and only through positive results in both steps does the patient receive the definitive diagnosis of a positive HIV sample [5].

Faced with an indeterminate result, the risk-benefit ratio of indicating the procedures to reduce vertical transmission of HIV should be considered, together with the pregnant woman [6].

Eventually, false-positive results may occur. False positivity in testing is more frequent in pregnancy than in children, non-pregnant men and women and can occur in some clinical situations, such as in the case of autoimmune diseases. To exclude the diagnosis of HIV infection in cases of suspected false-positive results, testing should be repeated on a new sample [6].

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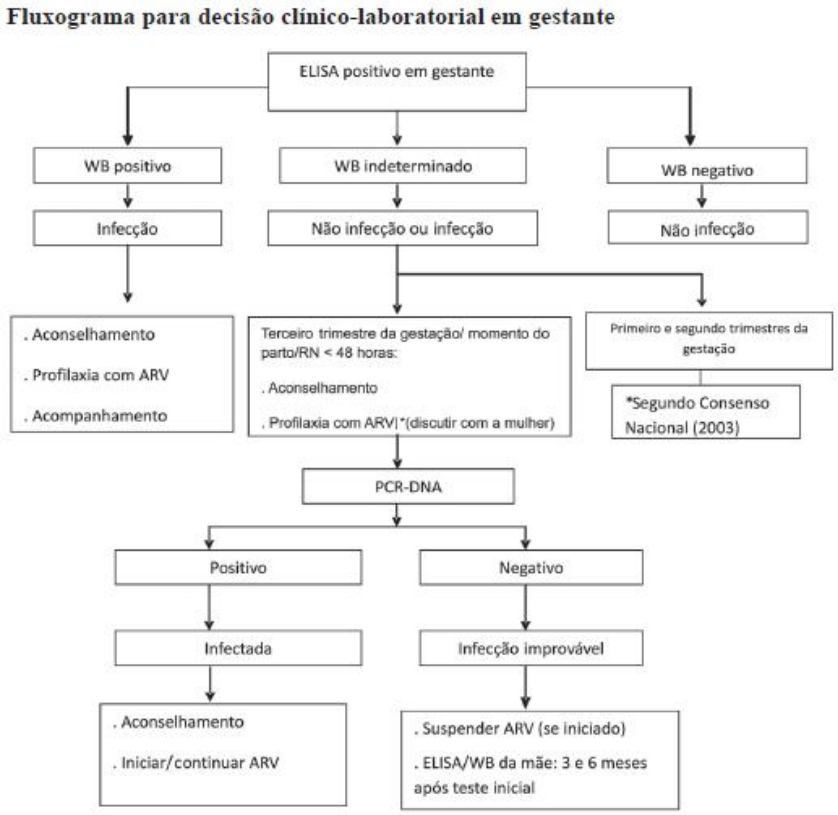

Fig.2: Flowchart for clinical and laboratory decision in pregnant women.

Source: Febrasgo [1].

The rapid HIV test has high sensitivity and specificity and, therefore, high rates of false positives in low-prevalence populations, such as pregnant women. It is reserved for cases in which the pregnant woman did not collect HIV serology during the prenatal period, in situations in which there is no access to the test result or when the patient is at risk of constant exposure and has not repeated the serology at the end of pregnancy. The patient's verbal consent for the examination is mandatory [5]. The following rapid tests have been validated: Rapid Check HIV 1 & 2TM; Rapid HIV Test 1 / 2TM - Biomanguinhos; Determine HIV 1 / 2TM; Unigold HIV TM; BD Check HIV Multi-test; HIV 1/2 Colloidal Gold.

The sample with a non-reactive result in the rapid test 1 (TR1) will be defined as “Non-Reagent Sample for HIV”. In this case, the diagnosis of the infection is completed, and there is no need to perform any additional tests [6].

Samples with reagent results in TR1 should be subjected to rapid test 2 (TR2). When available at the health service, the rapid immunoblot can also be used as TR2 [6].

Samples with reagent results in TR1 and TR2 will have their result defined as: “Sample Reagent for HIV” without the need for any additional tests [6].

Samples with discordant results between TR1 and TR2 will not have their result defined. In this case, the report will not be released and a new sample must be collected by venipuncture and submitted to the flow chart. If the definitive diagnosis is not established, the doctor and the pregnant woman must jointly define the conduct, considering the risk-benefit relationship and including the use of other diagnostic methods [6].

What concerns should the medical team take?. All members of the medical team participating in invasive procedures, including surgical or obstetric procedures, must use appropriate barrier precautions to avoid contact with the skin and mucosa with the blood and other body fluids of all patients. Gloves, surgical masks and goggles should be used in all invasive procedures that commonly result in the generation of droplets, blood and other body fluids, or bone fragments. Liquid-resistant cloaks or aprons that provide an effective barrier should be used.

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In the event that any member of the team is exposed or punctured with a needle, prophylactic treatment must be initiated. As an important addendum to the safety of medical staff, unfortunately, if guidance on these precautions is reserved for women who are known to be HIV positive, a large number of women with incubated or asymptomatic infections, who are not diagnosed, will pose a greater threat to medical team.

How to proceed with treatment. The two main categories of antiretrovirals (ARV) are: those that inhibit the viral enzyme reverse transcriptase and those that inhibit the enzyme viral protease. Reverse transcriptase inhibitors may be non-nucleoside (NRTI), such as zidovudine (AZT) and lamivudine, or nucleoside (NRTI), such as nevirapine. They block the HIV replication cycle in RNA-dependent DNA synthesis (reverse transcription). Inhibitors of the viral protease enzyme prevent virions, formed within the infected cell, from being released to infect new cells. An example of ARVs in this group is ritonavir [12].

Current recommendations for the use of antiretroviral therapy (ART) in pregnancy are quite aggressive and use broader criteria for indication than for adults in general. This is due to the objective of achieving undetectable viral load at the end of pregnancy and the consequent benefit of non-vertical transmission. However, it is questioned whether the "prophylactic" use of antiretrovirals would not harm the future treatment schemes for this patient, outside the gestational period. On the other hand, it is known that, after delivery of women without ART or using AZT, there is a rebound effect with an increase in viral load that reaches levels higher than those observed pre-treatment. Stopping or continuing ART in the puerperium, an increase in viral load is observed in the period, suggesting that the physiological changes in pregnancy are responsible for this increase in viral load (CV). Women who received ART during pregnancy have a lower risk of developing AIDS in the postpartum period, regardless of therapy [1].

It is necessary to be clear the difference between the institution of antiretrovirals in pregnant women with the aim of preventing vertical transmission - prophylactic TARV - and the institution of this therapy because there is an indication for the compromised clinical and / or immunological status of the woman - ART treatment. Women on antiretrovirals, under ART prophylaxis, may have this therapy suspended at the end of pregnancy. This assessment should be carried out, preferably, in the first 2 weeks postpartum, in a specialized service [1].

The indications for starting ART treatment in pregnant women follow the same principles as for non-pregnant patients: clinical manifestations or complications resulting from HIV-associated immunodeficiency, regardless of CD4 count and plasma viral load and T-CD4 lymphocyte count <200 / mm3 [1].

The goal of prophylactic ART in pregnant women is to achieve undetectable CV, thus reducing the risk of VT. The scheme with the best results in reducing viral load should be offered, which unleashes the least potential for maternal and fetal toxicities and has the least risk of inducing viral resistance [1].

The first clinical study that used antiretroviral therapy in order to reduce rates of vertical HIV transmission was Protocol 076, from the Pediatrics Aids Clinical Trial Group (PACTG 076). This was a randomized, placebo-controlled study that used a protocol consisting of oral zidovudine (AZT) from the 14th week, intravenous AZT (EV) 4 hours before delivery and AZT oral solution for the newborn, for 6 weeks [6].

This intervention reduced the rate of vertical HIV transmission by 67.5%. Vertical transmission rates were 25% in the placebo group and 8.3% in the group that received the AZT intervention. In PACTG 076, the development of viral resistance to zidovudine monotherapy was observed in approximately 2.7% of patients [6].

The effect of AZT on HIV viral load is not the only factor responsible for reducing vertical transmission. Studies of placental perfusion have shown that AZT is metabolized to active triphosphate within the placenta, which could be responsible for additional protection against intrauterine transmission.

In comparison with other antiretrovirals, resistance to zidovudine develops slowly, especially when associated with high viral load. Resistance has not been found in women who have used shortened regimens of these drugs to prevent vertical HIV transmission [6].

The use of regimens combined with two antiretrovirals (dual therapy) showed a five-fold reduction in the rate of vertical transmission compared to the results of AZT monotherapy. Dual therapy consisted of the association between zidovudine and lamivudine.

In the Ministry of Health Manual [6], a study published in 2002, evaluating 1,442 pregnant women, showed the following vertical transmission rates: 20% in the absence of ART, 10.4% with AZT monotherapy, 3.8 % in dual therapy and 1.2% in highly active regimens (combination of three ARVs or HAART - high potency antiretroviral therapy). Other studies have confirmed this hypothesis.

The HIV-NET 012 randomized clinical trial, which compared nevirapine versus oral zidovudine administered at the beginning of labor and in newborns, showed that

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perinatal HIV transmission rates were lower in the group receiving nevirapine (13.1% vs 21.5%; p <0.001), RR 0.58 (95% CI 0.40-0.83). However, nevirapine resistance can be induced by a single genotypic mutation, detected in 15% of women in six weeks postpartum, making it impossible to use this drug or any other protease inhibitor later, and for this reason, it should be used only if there is no other alternative (evaluate risk-benefit).

The goal of reducing vertical transmission means that every HIV-infected pregnant woman is treated with potent antiretroviral therapy, regardless of her immunological or virological status. The prophylactic use of ARVs should be started from the 14th week of pregnancy; the start of ARVs is not an emergency, and clinical and laboratory evaluations must be carried out prior to the start of ART, except in pregnant women who start care in advanced pregnancies (more than 28 weeks) or in those who use recreational drugs or co-infections that can disturb the placental barrier and increase the risk of VT. In these situations, the initiation of ART should be carried out even before obtaining the results of the pre-treatment tests, which should ideally be collected before the initiation of ART [1].

Women who have already received ARV prior to pregnancy should be informed about the potential risks / benefits of maintaining, modifying or suspending treatment, with regard to the evolution of their own disease. In addition, the potential adverse effects of ARV therapy on the child should be considered. The conduct should be decided, case by case, by the obstetrician and clinician / infectologist, together with the pregnant woman. In general, it is recommended that if the woman is not using therapy known to be associated with teratogenicity to the fetus (mainly efavirenz), the need to maintain ART to benefit the pregnant woman and, indirectly, maintain virological control and TV reduction [1].

The Ministry of Health Manual [6] recommends:

> Due to its potential to inhibit viral replication, lower risk of viral resistance in the short term and greater safety of antiretrovirals, ART should be administered to all HIV-infected pregnant women, with the association of three antiretrovirals, regardless of virological, clinical or immunological.

In addition to the appropriate antiretroviral treatment, other measures were necessary and contributed to the great decrease in the vertical transmission rate in recent years: anti-HIV examination during pregnancy and counseling for pregnant women; adequate prenatal care; and elective cesarean section when the viral load was high.

The prohibition of breastfeeding, with the provision of milk formula for the newborn, is also an important measure of reducing vertical transmission of HIV [13].

In children fed with breast milk, the effectiveness of antiretroviral has been reduced to about 30%. There is no doubt that the use of ARVs during pregnancy has been the factor with the greatest impact in reducing the rate of vertical transmission in recent years (Brocklehurst). There are, however, some studies that show the possible side effects in pregnant women and newborns (NB) who are submitted to this practice [13].

In addition to antiviral treatment to prevent vertical transmission, prenatal care should include counseling and aspects of contraception to avoid future pregnancy.

However, in the guidance on contraception we must remember:

> Although HIV infection is sexually transmitted, and vertical transmission of the virus may also occur, infected women have the same reproductive rights as all others, recognized by foreign and national legislation. These recommendations establish the right of every couple to decide freely and responsibly about their reproduction, and to have access to information on ways to do so and how to have a healthy and safe sex life, free from discrimination or violence [14].

Regarding the adverse effects of antiretrovirals during pregnancy, the Ministry of Health Manual [6] states that:

> The adverse effects rarely determine the suspension of the use of ARVs, since the effectiveness of these drugs in preventing vertical transmission of HIV, clearly outweighs the risks of adverse reactions to them.

The physiological changes that occur during pregnancy can affect the kinetics of drug absorption, distribution, biotransformation and elimination, potentially changing the pregnant woman's susceptibility to toxicity to different drugs [6].

Among the antiretrovirals available, zidovudine (AZT) and the one that most presents data related to pregnancy safety; information about other antiretrovirals is limited [6].

With the use of AZT we can observe spinal toxicity, macrocytic anemia (severe when Hb <8 g / dl) and

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neutropenia (severe when leukocytes <1.000 cells / mm3) [4].

The use of ARVs during pregnancy can cause side effects similar to those seen in any patient, such as mitochondrial toxicity, hypersensitivity reaction and lipodystrophy. In addition to these effects, there are other possible consequences and exclusively related to the use of ARVs during pregnancy [13].

Table 1 lists in which category ARVs are classified by the Food and Drug Administration (FDA) and whether or not there is a transplacental passage.

Table 1 - Antiretrovirals, FDA pregnancy categories and transplacental passage.

Antiretroviral	FDA (Food and Drug Administration) Gestation Categories	Passage through the placenta
Nucleoside and nucleotide analog reverse transcriptase inhibitors (ITRN and ITRN +)		
Abacavir	C	Yes (rats)
Didanosine	B	Yes (human)
Lamivudine	C	Yes (human)
Stavudine	C	Yes (human)
Tenofovir	B	Yes (human)
Zidovudine	C	Yes (human)
Non-nucleoside analog transcriptase inhibitors (NRTIs)		
Efavirenz	B	Yes (rats, rabbits)
Nevirapine	D	Yes (human)
Protease inhibitors (IP)		
Atazanavir	B	Yes (human)
Darunavir	B	Ignored
Fosamprenavir	C	Ignored
Indinavir	C	Yes (human)
Lopinavir / ritonavir	C	Yes (human)
Saquinavir	B	Yes (human)
Fusion Inhibitors		
Enfuvirtide		Ignored
Integrase Inhibitors		
Raltegravir	B	Yes (rats, rabbits)

Source: Adapted From Recomendations for use Of Antiretroviral Drugs In Pregnant Hiv Infected Women For Maternal Helth And Interventios To Reduce Perinatal Hiv Transmission In The United States (2008).

In a study carried out by Alcântara et al [15] on situations that make it difficult for pregnant women to adhere to treatment, it was shown:

Women reported difficulties in accepting the diagnosis of HIV, especially when it occurred during pregnancy, a situation that

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> negatively impacted treatment adherence. It was also possible to verify from the interviewees' statements that feeling healthy, without any signs or symptoms indicative of AIDS, was a reason for not adhering to the treatment. The side effects of medications are the main reasons for giving up antiretroviral therapy and there is an association between improvement of symptoms and abandonment of treatment. Conditions that motivated the pregnant woman to follow the treatment were the fears experienced by pregnant women both of transmitting HIV to the baby and of not following the growth of their children.

Among the general adverse effects, Mirochnick, Best, Clarke [12] in "Antiretroviral pharmacology: special issues regarding pregnant women and neonates", identify mitochondrial toxicity. According to these authors, this type of toxicity is common among reverse transcriptase inhibitors (NRTI and NRTI). Signs and symptoms such as myopathy, neuropathy, fatty liver and lactic acidosis may appear. The treatment is to stop using the causative drug and, sometimes, other drugs that can exacerbate the symptoms caused by ARV 10 [13].

Barros et al [13] in the study "Use of Antiretrovirals in Pregnancy and its Possible Adverse Effects" deal with hypersensitivity. The drugs that are most commonly related to symptoms are non-nucleoside reverse transcriptase inhibitors (NRTI), such as nevirapine and abacavir, and protease inhibitors (IP), amprenavir and tipranavir. It usually manifests itself through a confluent, erythematous, maculopapular, pruritic skin rash, which may or may not be accompanied by fever. Around 50% of cases resolve spontaneously, regardless of continued ARV therapy. Each case must be assessed individually for the treatment decision. In mild to moderate cases, it is possible to choose to continue using the drug, with the concomitant use of antihistamines [13].

Barros et al [13] also recognize lipodystrophy. That for these actors it is a redistribution of fat in the body and can be caused by NRTI or IP. This redistribution can cause a decrease in fatty tissue in some places (lipoatrophy) and gain in others (hyperadiposity). Lipoatrophy is more common on the face, limbs and glutes, and hyperadiposity is more common on the back, abdomen and breasts, and lipomas may appear. The lipodystrophy syndrome is when the patient presents this alteration associated with another metabolic disorder, such as dyslipidemia, hyperglycemia or lactic acidosis. The incidence of metabolic disorders is higher among patients treated with PI [13].

There is no specific treatment for lipodystrophy syndrome. You can try changing the medication, such as changing an IP by an NRTI. The results of these changes are, however, uncertain. Patients should also be encouraged to maintain a healthy diet and exercise [12].

As for the adverse effects related to pregnancy, Barros et al [13] recognize glucose intolerance or gestational diabetes. One of the recognized side effects of PI is insulin resistance (IR) and consequent glucose intolerance and hyperglycemia. IR is the state in which a higher concentration of insulin is needed to achieve a normal biological response. The drugs indinavir and lopinavir / ritonavir (Kaletra®) can induce IR, while nelfinavir and atazanavir do not appear to have this effect [13].

Some studies have attempted to predict the relationship between PI and gestational diabetes (GDM), since there is a clear relationship between these drugs and glucose intolerance outside pregnancy. DMG affects between 2 and 5% of pregnancies and occurs due to IR mediated by placental hormones, such as the placental lactogenic hormone and the placental human growth hormone. However, these studies proved inconclusive regarding the association between the use of PI during pregnancy and the development of gestational diabetes. If the use of PI is considered necessary in the treatment of pregnant women, it is prudent to monitor blood glucose more carefully during pregnancy [13].

Santos et al [4] claim that:

> Protease inhibitors can have the following adverse effects: elevation of total cholesterol, low-density lipoprotein (LD) and triglycerides; greater atherogenic action; hyperglycemia. These aspects increase the risks of systemic arterial hypertension (SAH), gestational diabetes and fetal macrosomia.

Figueiro, Coelho, Tamura [16] suggest:

> Pregnant women using certain antiretrovirals should be screened with greater emphasis on gestational diabetes and fetal vitality assessors (cardiotocography, Doppler and fetal biophysical profile) instituted early, starting at 28 weeks. The pregnant woman must also be accompanied on more frequent returns, seeking to actively combat genital infections and risk situations for preterm births.

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Barros et al [13] recognize ARV and pre-eclampsia as adverse effects related to pregnancy. Preeclampsia complicates about 3% of pregnancies, and is one of the major causes of maternal and perinatal morbidity and mortality, especially in developing countries. Some studies have tried to demonstrate the association between the onset of pre-eclampsia and the use of ARV for prophylaxis of vertical HIV transmission. Despite very controversial findings in different studies, there seems to be no strong association between the use of ARV and preeclampsia during pregnancy. Some studies suggest that HIV infection may decrease the prevalence of preeclampsia due to incompetence of the immune system. With the use of ARVs, the prevalence is equivalent to that found in uninfected patients, considering that the competence of the immune system is restored [13].

Barros et al [13] report the adverse effect of Teratogenicity related to the use of ARV. The treatment of HIV infection with ARV during pregnancy has been a very common and effective practice, used in recent decades to reduce vertical transmission of the virus. This practice has led to the current concern with the possibility of a teratogenic effect due to the use of these medications, prophylactically, during pregnancy. Efavirenz has been associated with neural tube malformations in baby monkeys exposed to medication for some years, but most studies in humans are inconclusive [13]. Most studies have shown no association between the use of ARV and fetal malformations. The use of AZT in the first trimester was associated with an increased risk of hypospadias in male fetuses. It should be noted, however, that in the last decades there has been an increase in the incidence of hypospadias, and this association may be just a correspondence to the world trend.

Santos et al [4] contraindicate the use of some ARVS and affirm its deleterious effects:

> Efavirenz: anencephaly, anophthalmia, microphthalmia, cleft palate, myelomeningocele. Amprenavir: fetal alcohol syndrome. Tenofovir: osteomalacia (study in animals). Indinavir: associated with hyperbilirubinemia and nephrolithiasis.

In a study by Lopes et al [17] comparing fetal structural and / or functional changes to ultrasound and echocardiography and perinatal results in pregnant women seropositive for the human immunodeficiency virus (HIV) in relation to a control group of patients attended by low-risk prenatal care, he discussed his findings:

> We prospectively evaluated 109 HIV-positive pregnant women using antiretrovirals and 200 control pregnant women, with monthly obstetric ultrasound monitoring and fetal and postnatal echocardiography performed with the assessment of amniotic fluid volume, weight adequacy. the presence of fetal structural changes and perinatal results. As relevant results, a higher prevalence of fetal heart disease and changes in the amount of amniotic fluid were observed in the studied group compared to the control group. Fetal and perinatal echocardiographic evaluations showed four cases (3.7%) of heart disease in the study group and none in the control group. Thus, although there were no differences for malformations as a whole, when we considered only heart diseases, there was a significant difference.

Considering their findings, Lopes et al [17] suggest:

> Thus, it should be noted that routine fetal echocardiography is indicated in HIV seropositive patients on ART.

There is still an adverse effect of hepatotoxicity related to the use of ARV during pregnancy. A randomized clinical trial, comparing nelfinavir and ne¬virapine, showed severe hepatic adverse effects in pregnant women with a CD4 + T-cell count greater than 250 cells / mm3, using nevirapine [13]. According to Barros et al [13], in a retrospective study published in 2005, there was a significant association between the use of nevirapine and the increase in liver enzymes during pregnancy. Such an association was not significant in non-pregnant women. In another Brazilian, he showed liver toxicity in 5.6% of the patients using nevirapine, with a case of Steven Jonhson's Syndrome [13].

About ARV, prematurity and low birth weight, Barros et al [13], explain that perinatal adverse events related to the use of ARV have been questioned by several authors.

A possible association between ARV use and prematurity was initially detected in 1998, when the observation of the occurrence of ten preterm infants in 30 women using ARV therapy was published in a Swiss study. A combined analysis of the European and Swiss study confirmed the increased risk of early delivery in the group of women using combined ARV therapy, compared to women without treatment. There was also an association with a higher occurrence of prematurity in patients using

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HAART therapy compared to those using therapy with only one or two ARVs [13].

Barros et al [13], complement that several studies have been done in this sense, however, the association between prematurity and low weight with the use of ARVs during pregnancy remains controversial. On the other hand, it appears that the birth of low birth weight neonates, in pregnant women who have been treated with HAART therapy, is more frequent. However, there is no doubt about the great benefit of combined ARV therapy in reducing vertical transmission, which should continue to be used, taking into account the neonatal risks and future benefits for these children. Pregnant women must have careful postnatal care, since prematurity and low weight are factors that significantly increase perinatal morbidity and mortality.

Figueiro, Coelho, Tamura [16] agree

> In a study evaluating the effect of antiretroviral drugs and their association with changes in the anthropometric parameters of neonates of pregnant women with HIV-1, it was observed that there was no difference between the Control Group compared to the group using zidovudine and the group who used the combination of zidovudine with lamivudine and nelfinavir with regard to the duration of pregnancy, Apgar score and neonatal anthropometric classification. There was also no increase in the incidence of preterm births in pregnant women who received the combination of antiretroviral drugs containing a protease inhibitor.

The Febrasgo High Risk Pregnancy Manual [1] clarifies about antiretrovirals in prenatal care. Every HIV-infected pregnant woman should receive ART during pregnancy. It is necessary to detect the difficulties of understanding on the part of the patient in relation to the use of medications, as well as other possible obstacles to her adherence to the treatment, guaranteeing her access to clear information about the objectives of the treatment; the meanings of viral load tests and CD4 + T lymphocyte count; the need to adhere to the proposed therapeutic regime; the potential adverse effects for the mother and fetus; the drugs that make up the scheme and its mechanisms of action; the importance of avoiding the use of alcoholic beverages and recreational drugs; the importance of the systematic use of condoms and the need for periodic consultations and exams in the segment [1]. Every pregnant woman should use potent ART as a prophylactic or initial therapy regimen, regardless of her immunological or virological status. Currently, the use of AZT monotherapy is no longer recommended, as this regimen does not offer good control of maternal viremia, which is the factor most strongly associated with VT. Following data from ART recommendations in adults, the AZT / 3TC association was maintained as the pair of nucleoside analogs of first choice to compose the initial ARV scheme. In cases of AZT intolerance, enteric didanosine (DDI EC) or tenofovir remain as substitution alternatives, always associated with 3TC [1].

Due to the adverse effects of efavirenz, mainly due to its teratogenicity, it is no longer the third preferred drug in the regimen for pregnant women. Since nevirapine has been associated with serious side effects, mainly allergy and hepatotoxicity in women with a high CD4 level (greater than 250), it was preferred to use protease inhibitors as the third preferred drug in the regimen, according to the Febrasgo High Risk Gestation Manual [1].

Thus, the preferred regimen of prophylactic ART during pregnancy or the first therapeutic regimen will be the use of AZT + 3TC + lopinavir / ritonavir, based on experience of use, in the largest number of clinical studies with this protease inhibitor and in high potency and durability of that ARV scheme. In the event of intolerance to lopinavir, atazanavir is a safe and effective alternative, always associated with ritonavir [1].

For Bassichetto et al [18] PIs should always be combined with ritonavir as a pharmacological adjuvant, which has the advantage of providing higher and more stable IP blood levels for a longer time, which determines a low risk of mutations that confer resistance viral.

In practical terms, after the 14th week of gestation, the use of prophylactic ARVs to reduce HIV-1 VT is indicated, and should be instituted as soon as the laboratory tests of liver function show that its use can be started. If the patient is being treated for HIV-1 infection, it is not advisable to stop the treatment because of the pregnancy, just adjust it. If zidovudine is not part of the scheme used, it is suggested to introduce it [9].

According to Duarte et al [9]:

> The combination of two reverse transcriptase inhibitors (zidovudine and lamivudine) is marketed in the Brazilian market in a single product (zidovudine 300 mg tablet + 150 mg lamivudine), administered orally, twice daily. The protease inhibitors recommended for preferential use in pregnant women are a

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combination of two drugs in this group (200 mg lopinavir tablets + 50 mg ritonavir tablets) and two tablets are administered orally twice daily. This guideline has also been adopted by the Brazilian Ministry of Health's National STD / AIDS Program.

According to the Frebasco "High Risk Pregnancy Guidance Manual - Human Immunodeficiency Virus Infection in Pregnancy" [1] in the event of a non-virological response after the introduction of ART, the patient should follow ART recommendations in adults and whenever possible, these cases should be conducted after genotyping prior to switching to a new ART scheme. It is argued that all pregnant women should be genotyped before the introduction of the first ARV regimen, aiming mainly to avoid the onset of an inadequate or flawed regimen and that increase the risk of virological non-suppression and the possibility of fetal / newborn resistant strain TV. This is still a consideration not fully supported by the Brazilian Ministry of Health, due to the low occurrence of primarily resistant strains in our population.

Table 2 summarizes the antiretroviral therapy recommendations during prenatal care, following the guidelines of the Ministry of Health [6].

Table 2 - Recommendations for prophylaxis of vertical HIV transmission and antiretroviral therapy in pregnant women.

Gestational Age	**Pregnant Woman's Clinical and Laboratory Status**	**Medical Conduct**
Between 14 and 28 weeks of gestation	symptomatic, with LT-CD4 + count ≥ 350	Combined ART prophylaxis (combination of three ARVs)
After 28 weeks of gestation	Asymptomatic, no LT-CD4 + count available	Collect blood for LT-CD4 + and CV counts, immediately start prophylaxis with combined ART (association of three ARVs) regardless of LT-CD4 + and CV results
<14 weeks and LT-CD4 + count close to 350 cells / mm³	Asymptomatic, with LT-CD4 + count between 200 and 350 cells / mm³	Entering ART after 14 weeks of gestation
<14 weeks and LT-CD4 + count close to 200 cells / mm³	Asymptomatic, with LT-CD4 + count between 200 and 350 cells / mm³	Introduce ART and maintain after delivery
Regardless of the IG	Asymptomatic, with LTCD4 + <200 cells / mm³	Introduce ART, maintaining after delivery. Introduce chemoprophylaxis for opportunistic infections
Regardless of the IG	Symptomatic	Introduce ART, maintaining after delivery. Introduce chemoprophylaxis for opportunistic infections

Source: Brasil [6].

Table 3 summarizes the choice of drugs used to start ART during pregnancy.

Table 3 - Medicines and scheme to start ART during pregnancy.

Pharmacological group	First choice	Second Choice
2 ITRN	AZT + 3TC	ddl EC + 3TC or d4T + 3TC
IP	LPV/r	SQV/r
AZT - Zivodudine; ddl EC - enteric didanosine; 3TC - lamivudine; d4T - stavudine; NVP - Nevirapine. LPV - Lopinavir; r - ritonavir as a pharmacological adjuvant; SQV - saquinavir.		

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Brazil in the "Treatment Guide - Recommendations for Prophylaxis of Vertical HIV Transmission and Antiretroviral Therapy in Pregnant Women" [6] on childbirth care for HIV-infected pregnant women shows that several studies published before the introduction of highly active antiretroviral regimens demonstrated the benefit of elective cesarean section in reducing vertical transmission (VT) of HIV compared to other types of delivery. However, at the time these studies were carried out, the current combined regimens of three antiretrovirals (highly active regimens) were not yet used and the measurement of viral load levels was unknown. The Cochrane Group carried out a systematic review, published in 2005, to assess the effectiveness and safety of elective cesarean sections in preventing vertical transmission. It was concluded that elective cesarean section was an effective intervention for the prevention of vertical transmission of HIV, in women who did not use ARV during pregnancy and in those who used only AZT.

The studies conducted so far have not shown differences in vertical transmission rates when comparing elective cesarean section and vaginal delivery in preventing HIV transmission, when the viral load is less than 1,000 copies / ml in pregnant women who are using a combined antiretroviral regimen. The elective cesarean section is the one performed before the beginning of labor, with the integral amniotic membranes. It is indicated for HIV seropositive pregnant women, when they have viral load ≥1.000 copies / ml or unknown, after 34 weeks of gestation.

Duarte et al [9] remember about the causes of placental lesions and amniorrexis in choosing the mode of delivery:

> In choosing the mode of delivery, it should be remembered that placental lesions and rupture of amniotic membranes are the main anexial factors that potentially increase HIV-1 VT, since they facilitate the virus's access to the fetus. In order to avoid these changes, it is important to note that smoking and the use of illegal recreational drugs cause placental microinfarctions. Additionally, all clinical situations related to premature rupture of the amniotic membranes must be remembered. Among these situations, the most frequent are genital and systemic infections and preterm labor.

The elective cesarean section should be scheduled for the 38th week of pregnancy, avoiding that the pregnant woman goes into labor and premature rupture of the amniotic membranes. Remember that pregnant women with HIV can go into labor one to two weeks before the expected date. Therefore, it is prudent to discuss this possibility with all pregnant women in the same situation, instructing them to seek maternity as soon as possible if they go into labor or if the amniotic membranes rupture. In the event that the pregnant woman goes into labor before the scheduled date for the elective cesarean, as long as the cervical dilation is less than 3 cm and the amniotic membranes are intact, the cesarean can be performed [6].

Duarte et al [9] agree:

> It is believed that cesarean sections performed at the beginning of labor still bring some benefit for the reduction of HIV-1 VT. In view of this practical assertion, it is tolerable that the item "out of labor" is not completely observed, accepting "labor still in its initial phase (2 to 3 cm of cervical dilation) does not contraindicate cesarean section as prophylactic measure of HIV-1 TV ".

The definition of the mode of delivery should be based on the result of the maternal viral load, carried out after the 34th week, in association with the obstetric evaluation [6]. In women with a viral load below 1,000 copies / ml, this definition can be discussed between the pregnant woman and her obstetrician, due to the observation that the type of delivery in these conditions, whether normal or operative, does not change the risk of vertical transmission of the baby. HIV, safeguarding the recommendations regarding the management of childbirth [6].

Elective cesarean section, in order to reduce vertical transmission of HIV, is indicated for pregnant women who, at the end of pregnancy (after 33-34 weeks), have an unknown viral load or greater than 1.000 copies / ml. When the viral load is less than 1.000 copies / ml, the mode of delivery will be defined by exclusively obstetric criteria.

Therefore, elective cesarean section should be indicated for HIV + pregnant women who did not undergo combined antiretroviral prophylaxis during pregnancy, who used only AZT monotherapy or who have their viral load, at 34 weeks or more of gestation, unknown or greater than 1,000 copies / ml [6].

For pregnant women who arrive at the maternity hospital in labor and who have not taken antiretroviral prophylaxis during pregnancy, the indication of the mode of delivery should take into account the stage of labor in which the mother is and the prognosis of the time of evolution for

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delivery, as well as the likelihood of complications during delivery. When labor is in rapid evolution, with a rapid birth prognosis, vaginal delivery should be indicated, using all precautions to reduce the risk of HIV transmission. If the labor is in its initial phase, with 3-4 cm of dilation of the uterine cervix and the amniotic pouch is complete or with a rupture of less than 2 hours, the cesarean section should be indicated immediately, to reduce the risk of VT during labor [6].

Brazil in the "Treatment Guide - Recommendations for Prophylaxis of Vertical HIV Transmission and Antiretroviral Therapy in Pregnant Women" [6] recommends the following general care in labor and delivery: 1. Administer intravenous AZT from the beginning of labor until birth and clamping of the umbilical cord. All pregnant women in labor should receive AZT, including those who did not use it during pregnancy and those who presented toxicity to it orally; pregnant women hospitalized for sedation of preterm labor must receive AZT EV while they are experiencing uterine contractions; 2. Clamp the umbilical cord immediately after birth, without performing milking; 3. Avoid invasive procedures during pregnancy, labor and delivery, such as cordocentesis, amniocentesis, amniotomy, the use of forceps and vacuum extractor; 4. In vaginal delivery, avoid episiotomy whenever possible; 5. Monitor labor, using the partogram, avoiding repeated touches; 6. In case of early rupture of the amniotic membranes during labor, assess the prognosis of evolution and use oxytocin, if necessary, to avoid prolonged labor with an increased risk of vertical transmission. If oxytocin is contraindicated and prolonged labor is foreseen, caesarean section may be indicated (1, A); 7. After birth, the woman and the newborn, being in good health, can be referred to joint accommodation.

For Duarte et al [9], patients who evolve to normal delivery, it is necessary to wash the vaginal canal, right after the diagnosis of labor is confirmed:

> Defining that the mode of delivery will be vaginal, when the patient goes into labor, a series of small interventions must be carried out. Despite divergent opinions regarding the effect of washing the birth canal on the effective reduction of HIV-1,8,12 VT, it is known that it reduces this complication in cases of amniorrexis with more than four hours of evolution. For other authors, washing the vaginal canal with 0.4% chlorhexidine is associated with reduced perinatal transmission of this virus. As it is not possible to predict which patient will have amniorrhexis whose labor exceeds this time, some services adopt such conduct, instituting the washing of the vaginal canal shortly after establishing the diagnosis of labor in the woman infected with HIV-1, in order to remove all vaginal content. The substance used can be polyvinylpyrrolidone-iodine, chlorhexidine or benzalkonium chloride.

Every HIV-positive pregnant woman should receive an intravenous infusion of AZT at the beginning of labor until the birth of the newborn, regardless of the antiretroviral regimen used in prenatal care, and the level of viral load [6]. Antiretrovirals in use during prenatal care should be continued during the period of hospitalization for delivery, following the original medical prescription regardless of the prescribed fasting period and the use of injectable AZT, to maximize the protective effect of vertical transmission and to reduce the risk of developing resistance to antiretrovirals. If it is possible to stop taking medications after delivery (ARV for prophylactic purposes), all drugs should be suspended together, except for regimens containing nevirapine, which should be phased out: initially, remove nevirapine, maintaining AZT and 3TC for a period of one to two weeks, according to the "Recommendations for antiretroviral therapy in HIV-infected adults - 2008". If the pregnant woman is using stavudine, this medication should be discontinued before the administration of intravenous AZT [6].

For pregnant women with indication for elective cesarean section, the AZT infusion should start 3 hours before surgery and be maintained until the time of birth.

HIV positive patients who arrive at the maternity hospital in labor, and who have not taken ARV prophylaxis during pregnancy, will immediately start using intravenous AZT and the newborn will receive AZT orally, starting within 2 hours. after birth.

Duarte et al [9] explain the intravenous AZT dosage in the peri-delivery period:

> In cases where the mode of delivery will depend only on obstetric criteria, as soon as the pregnant woman enters labor, zidovudine should be administered intravenously at a dose of 2 mg / kg of weight, followed by continuous infusion at a dose of 1 mg / kg body weight / hour until delivery, regardless of having used ARV during prenatal care. In cases of elective cesarean section, it is advisable to start the

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AZT infusion three hours before beginning the surgery, with hourly peaks of 1 mg / kg of weight.

The Febrasgo High Risk Gestation Manual [1] recommends the same dosing schedule as PACTG 076, thus disagreeing with Duarte et al [9] with regard to the attack dose in elective cesareans, as it deems it necessary.

Table 4 - AZT dosing schedule for the parturient woman.

PACTG 076 - Dosing schedule for AZT in parturient women
AZT for injection - 200 mg vial with 20 mL (10 mg / mL): the parturient You should receive AZT intravenously, from the beginning of labor until the clamping of the umbilical cord. Dose: start the infusion, in individualized venous access, with 2 mg / kg in the first hour, following a continuous infusion with 1 mg / kg / h, until the umbilical cord is clamped. Dilute in 5% glucose serum and drip, as appropriate. The concentration should not exceed 4 mg / mL. Note: this recommendation refers to all types of delivery, including elective cesarean section, and this starts AZT, IV, 3 hours before the surgical intervention.

Source: Febrasco [1].

Table 5 - Dilution of zidovudine considering the loading dose and maintenance doses, according to the weight of the pregnant woman and the desired concentration. In the example in this table, 100 ml of 5% glucose serum will be used, remembering that each ml of the zidovudine ampoule has 10 mg of the drug.

Pregnant weight

Dose	**Variables**	**40 kg**	**50 kg**	**60 kg**	**70 kg**	**80 kg**	**90 kg**
Attack (2 mg / kg) Run in the first hour in 100 ml	Amount (mL) of zidovudine.	8	10	12	14	16	18
	Number of drops / min.	36	37	37	38	39	39
Maintenance (1 mg / Kg / hour) Continuous infusion in 100 mL	Amount (mL) of zidovudine. Number of drops / min.	4 35	5 35	6 35	7 36	8 36	9 36

Source: Duarte et al [9].

Other aspects regarding prenatal care must be considered. In prenatal care for HIV-positive pregnant women, the time of diagnosis must first be taken into account. The approach of the newly diagnosed patient differs in some aspects from the pregnant woman who already has the virus.

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Table 6 – Fundamental aspects in assisting HIV-positive pregnant women.

Chronic infection	Recent diagnosis
Check date of diagnosis and time of infection; Assess CD4 cell count and viral load already performed; Check history of opportunistic infections; Evaluate current and previous antiretroviral therapy; Guidance on preventing vertical transmission.	Advice on the natural history of the disease, prevention of new infections and prognosis; Psychological and social support; Assess the current status of the infection by measuring viral load and CD4; Guidance on antiretroviral treatment; Guidance on preventing vertical transmission.

The first consultation is extremely important, as in it the doctor must collect all the data necessary to understand the patient, in addition to guiding the possible risks that she runs, as well as the fetus.

Laboratory tests include basic prenatal examinations, plus the necessary tests to assess the progression of the disease, possible changes caused by antiretrovirals and serologies and tests for opportunistic infections. Possible adverse factors should be identified, such as smoking, use of intravenous drugs and alcoholism.

The initial physical examination should be as detailed as possible, with special attention to the systems most affected by HIV and the possible signs of immunodeficiency that they may show. The table below shows the main ones.

Table 7 - Signs of immunodeficiency.

Signs of Immunodeficiency
- Repeated vaginal candidiasis; - Oral and esophageal cadidiasis; - Atypical pneumonia; - Recurrent herpes zoster; - Extragenital contagious mollusk; - Recurrent cervical intraepithelial neoplasia (CIN); - Recurrent and atypical genital herpes.

Among the routine exams, the first consultation of the HIV positive pregnant woman should also contain:

1. CBC: monitoring the toxicity of antiretrovirals (mainly AZT);

2 CD4 cells: assessment and staging of the disease;

3. Liver and kidney function: monitoring the toxicity of antiretrovirals;

4. VDRL: HIV / Syphilis co-infection;

5. Hepatitis B and C: hepatitis C / HIV co-infection and hepatitis B vaccination;

6. Toxoplasmosis: Risk of reactivation, especially if the CD4 cells are below 100 / mm^3;

6. Rubella, urine culture, ABO blood group, RH factor, blood glucose: basic tests;

7. Cytomegalovirus (CMV): risk of reactivation;

8. PPD: positive test (> 5mm): perform tuberculosis prophylaxis;

9. Culture and / or PCR for chlamydia and gonococci: Not mandatory;

10. Cervico-vaginal oncotic cytology: screening for cervical intraepithelial neoplasia and cervical cancer.

The administration of vaccines with live attenuated viruses in pregnant women and / or patients with immunodeficiency is subject to individual risk-benefit analysis and should not be performed in case of severe immunodepression. In addition to the aspects that concern pregnancy, it is necessary to consider the immunological conditions of the pregnant woman. In HIV infection, as immunodepression increases, the possibility of a consistent immune response is reduced. The table below shows recommendations on vaccination for HIV-positive pregnant women.

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Table 8 - Vaccine administration.

Immunization	Recommendation
Vaccine for tetanus and diphtheria (dT)	Reinforcement indicated if the last dose was administered more than 05 (five) years ago. If the pregnant woman is not vaccinated or the vaccination status is unknown, indicate three doses (standard schedule).
Hepatitis B vaccine	Recommended for susceptible pregnant women (anti-HBs negative), at risk. The dose should be twice that recommended by the manufacturer: time 0, 1, 2 and 6 or 12 months.
Human immunoglobulin for hepatitis B virus (HBIG)	Recommended for susceptible pregnant women (anti-HBs negative), drug users who share syringes and needles, those who have unprotected sexual contact with HBsAg positive people or in the case of victims of sexual violence. It must be started within the first 14 days of exposure.
Hepatitis A vaccine	Recommended for susceptible pregnant women (anti-HAV negative) co-infected with hepatitis B or C. Perform two doses with an interval of 06 months.
Influenza	Recommended annually for those infected with HIV before the influenza period. Trivalent inactivated vaccine, one annual dose, can be given during pregnancy.
Immunoglobulin for varicella zoster virus (VZV)	Recommended for susceptible pregnant women (negative anti-VZV) after exposure to the home, hospital or close neighbors.

Source: Brasil [6].

IV. RESULTS - PROTOCOL OF THE OBSTETRIC CENTER OF HOSPITAL DE BASE DR ARY PINHEIRO

As a result of the research, a protocol was developed, which proposition to be followed by the professionals of the Obstetric Center of the Hospital de Base Dr. Ary Pinheiro (HBAP) in the management of patients with HIV during pregnancy.

This protocol is based on medical experiences, with renowned authors and bibliographic review on the subject. The protocols defined in each service are of paramount importance, since they establish rules to be followed by the professionals working, contributing to the same language in the treatment of patients, as well as in the transmission of knowledge to students, interns and resident physicians of the service. The proposed protocol is not intended to be the last word on the diagnosis and / or treatment of HIV in pregnancy, and can be modified when necessary, given that medicine is not an exact science and is constantly evolving.

4.1 Protocol - HIV in Pregnancy

Description: Classification of HIV infection:

A: Asymptomatic Acute Infection, lymphadenopathy

B: Symptomatic, No A, No C

C: Indicative conditions for immunodeficiency.

Table 9 - Indicative conditions for immunodeficiency.

Linfócitos T-CD4 (em cel/ml)	A	B	C
> 500	A1	B1	C1
200-499	A2	B2	C2
< 200	A3	B3	C3

A3, B3, C1, C2, C3 are defined as AIDS cases

Prenatal Serological Diagnosis: Request serology at the 1st prenatal consultation; if negative, repeat in the 3rd quarter.

The diagnosis is made before 2 ELISA tests (which detect antibodies to HIV1 and HIV2), confirmed by Western Blot (or immunofluorescence). The HIV serological test should always be requested with the patient's agreement; in case of refusal, record the fact in the medical record.

Rapid Test: Only used when the pregnant woman has not had prenatal care or when the test is not available; it is valid to guide intrapartum therapy.

Prenatal exams: Notification is mandatory (for both parturients and abortions), even in situations where the pregnant woman has already been notified as an AIDS case, it is mandatory to notify her as an HIV + pregnant

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woman using the specific forms - Notification and investigation form for HIV + pregnant women and exposed children.

1. Routine prenatal examinations at the first consultation of the HIV-positive pregnant woman:

• CBC, liver and kidney function (monitoring of ARV toxicity)

• VDRL, hepatitis B and C (HIV / Syphilis co-infection, hepatitis C / HIV;

• Toxoplasmosis and Cytomegalovirus (risk of reactivation, especially if CD4 cells are below 100 / mm3);

• Basic exams (Rubella, urine culture, ABO blood group, RH factor, blood glucose);

• PPD (Perform tuberculosis prophylaxis);

• Cervical-vaginal cytology.

2. Others that are necessary according to the associated pathologies.

3. Count of CD4 lymphocytes every quarter.

4. Quantification of viral load every quarter.

Pre-Christmas and Puerperium:

1. Early supplementation of iron and folic acid;

2. Guide the use of condoms in all intercourse during pregnancy;

3. Guide to quit smoking and illicit drugs;

4. Routine vaccination against tetanus and diphtheria (dT) (Booster indicated if the last dose has been administered more than 5 years ago. If the pregnant woman is not vaccinated or the vaccination status is unknown, indicate three doses), hepatitis B (Recommended for susceptible pregnant women, the dose should be twice that recommended by the manufacturer: time 0, 1, 2 and 6 or 12 months), H1N1 (Recommended annually for those infected with HIV before the influenza period. Trivalent inactivated vaccine. DO NOT PERFORM DOSING CD4 AND CV UP TO 4 WEEKS AFTER VACCINATION) and Hepatitis A vaccine (recommended for susceptible pregnant women co-infected with hepatitis B or C. Perform two doses at an interval of 06 months);

5. Human immunoglobulin for hepatitis B virus (recommended for susceptible pregnant women who have had unprotected sexual contact or drug users who have shared syringes and drugs with HBsAG positive people or in the case of victims of sexual violence. Must be started within the first 14 days exposure);

6. Immunoglobulin for varicella zoster virus (recommended for susceptible pregnant women, after exposure to the home, hospital or close neighbors);

7. Prophylaxis for Pneumocystis carinii pneumonia (PCP) is indicated in pregnant women with previous pneumonia, by CD4 below 200 and unexplained fever: Sulfametoxazol-Trimetropina (400mg / 80mg) 2 tablets a day 3 times a week, after the 1 trimester, stopping at 36 weeks;

8. Guide patients not to breastfeed.

Other Recommendations: Follow-up by a multidisciplinary team, in which the infectious disease specialist plays an important role in guiding antiretroviral medication, as well as in guiding prophylaxis and treating opportunistic infections (such as those caused by Pneumocystis and Toxoplasma gondi); Avoid invasive procedures, such as amniocentesis and cordocentesis; At each prenatal visit, pay attention to the presence of intercurrent gynecological infections, including HPV; Virological and immunological assessment tests should be performed periodically (viral load, CD4 and CD8), as well as blood count, kidney and liver function; Serologies indicating susceptibility should be repeated every quarter; If the pregnant woman already uses antiretroviral therapy, it should be maintained until the infectologist evaluates; drugs contraindicated in pregnancy should be replaced.

Drug Treatment in Pregnancy: Aiming only at prophylaxis of vertical transmission, treatment should be started from the 14th week of pregnancy. The recommended first choice regimen is Biovir® (AZT 300 mg + Lamivudine 150 mg) - 1 tablet orally every 12 hours combined with Kaletra® (Lopinavir 200 mg + Ritonovir 50 mg) - 2 tablets orally every 12 hours hours.

The following table summarizes the recommendations for ART during prenatal care.

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Table 10 - Recommendations for prophylaxis of vertical HIV transmission and antiretroviral therapy in pregnant women.

GESTATIONAL AGE	CLINICAL-LABORATORY STATUS OF THE PREGNANT	MEDICAL CONDUCT
Between 14 and 28 weeks of gestation	Asymptomatic, with LT-CD4 + count ≥ 350	Combined ART prophylaxis (combination of three ARVs)
After 28 weeks of gestation	Asymptomatic, no LT-CD4 + count available	Collect blood for LT-CD4 + and CV counts, immediately start prophylaxis with combined ART (association of three ARVs) regardless of LT-CD4 + and CV results
<14 weeks and LT-CD4 + count close to 350 cells / mm³	Asymptomatic, with LT-CD4 + count between 200 and 350 cells / mm³	Entering ART after 14 weeks of gestation
<14 weeks and LT-CD4 + count close to 200 cells / mm³	Asymptomatic, with LT-CD4 + count between 200 and 350 cells / mm³	Introduce ART and maintain after delivery
Regardless of IG	Asymptomatic, with LTCD4 + <200 cells / mm³	Introduce ART, maintaining after delivery. Introduce chemoprophylaxis for opportunistic infections
Regardless of IG	Symptomatic	Introduce ART, maintaining after delivery. Introduce chemoprophylaxis for opportunistic infections.

Source: Brasil [6].

Prophylactic schedule using AZT at the time of Childbirth: All pregnant women who enter the Hospital de Base Dr Ary Pinheiro should be asked for an HIV serological test.

In labor: Indicated for all patients, regardless of ART (Antiretroviral Therapy) used in pregnancy. Its presentation is a 20 ml vial with 200 mg (10 mg / ml) of AZT. Attack dose: 2 mg / Kg IV in the first hour (diluted in 100 ml of 5% SG) Maintenance dose: 1mg / Kg / hour IV until the umbilical cord is clamped In elective cesareans, start AZT at least 3 hours before withdrawal of the fetus. Do not exceed a concentration of 4 mg / ml.

Table 11 - Attack (2 mg / kg) - Run in the first hour - Preparation in 100 ml of SG5%.

Patient Weight in Kg	Qty of Zidovudine in ml	Number (drops / minute)
40	8	36
50	10	37
60	12	37
70	14	38
80	16	39
90	18	39

Table 12 - Maintenance (1mg / Kg / hour) - in continuous infusion - Preparation in 100 ml of SG5%.

Patient Weight in Kg	Qty of Zidovudine in ml	Number (drops / minute)
40	4	35
50	5	35
60	6	35
70	7	36
80	8	36
90	9	36

Delivery Way

1. Viral load below 1.000 copies / ml or undetectable, evaluated at around 34 weeks: vaginal delivery or the obstetric indication route;

2. Viral load above 1.000 copies / ml or unknown, assessed after 34 weeks: elective cesarean section (out of labor and intact membranes). Here cesarean section will also be indicated in the beginning of labor with intact membranes and cervical dilation up to 3 to 4 cm; (URGENCY CESÁREA DOES NOT REDUCE TV)

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3. The elective cesarean section should be scheduled for the 38th week of pregnancy, preventing the pregnant woman from going into labor and premature rupture of the amniotic membranes.

4. Regardless of viral load: advise cesarean in cases of premature labor THAT DOES NOT RESPOND TO INHIBITION, giving AZT IV for at least 1 ½ hours, reassessing cervical dilation.

Care in elective cesarean section

- 1. Administer AZT at least 3 hours before;
- 2. Maintain the ARVs taken by the pregnant woman while waiting for delivery, at the usual time, regardless of fasting (except stavudine - d4T - which must be suspended 12 hours before);
- 3. Follow cesarean technique with emphasis on removal of the fetus with intact membranes (impelled), if possible;
- 4. Clamp the cord immediately without milking;
- 5. Remove the maternal AZT IV;
- 6. Use antibiotic prophylaxis routinely.

Comments

In cases of delivery with very rapid evolution, the loading dose of AZT should be administered in 30 minutes.

In cases of elective cesarean sections, use AZT for 4 hours before the procedure.

Childbirth care - general rules

In cesarean section, perform a technique with rigorous hemostasis of all planes, including the lower segment, with removal of impelled fetus (if possible).

• Immediate clamping of the umbilical cord

• Immediate removal of blood and secretions in contact with the newborn's skin and mucous membranes

• Avoid prolonged labor

• Avoid amniotomy and prevent more than 4 hours of broken bag

• Do not perform forceps or episiotomy

• Remove AZT intravenously after clamping the cord

• Maintain the antiretroviral regimen in the puerperium, when indicated (if it is therapeutic, and not only prophylactic for vertical transmission).

Maternal, obstetric, fetal, attachment, viral and postnatal factors increase HIV VT. Table 13 summarizes the factors that increase Vertical HIV Transmission.

Table 13 - Factors that increase Vertical HIV Transmission

Maternal Factors	**Obstetric Factors**	**Fetal Factors**	**Annex Factors**	**Viral Factors**	**Postnatal Factors**
1. High maternal viral load; 2. Low T-CD4 lymphocyte count; 3. Reduction of neutralizing antibodies; 4. Acute infection during pregnancy; 5. Associated infections (genital and systemic infections); 6. Multiple sexual partnership; 7. Smoking; 8. Use of illicit drugs; 9. Not using antiretrovirals; 10. Unprotected sexual practice.	1. Prolonged rupture of membranes; 2. Exposure to maternal blood; 3. Invasive fetal propaedeutics; 4. Type of delivery (when viral load> 1,000 copies / ml).	1. Genetic susceptibility; 2. Reduced function of fetal cytotoxic lymphocytes; 3. Integrity of the skin and mucous membranes; 4. Prematurity.	1. Expression of HIV receptors in the placenta; 2. Loss of placental integrity.	1. Viral phenotype; 2. Resistance to ARVs; 3. Macrophage tropism.	1. Natural breastfeeding.

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V. FINAL CONSIDERATIONS

There are countless pathologies that can be present during the woman's pregnancy and, thus, cause harmful effects on the mother-fetus binomial. HIV is a worldwide problem, and, as far as infected pregnant women are concerned, we have one more concern. In addition to the morbidity and mortality caused by the disease, we are afflicted by the risk of vertical transmission.

When the pregnant woman arrives for prenatal care, she often does not even know how to be infected with HIV. The first opportunity to avoid vertical transmission is made by ordering anti-HIV tests early, making pre and post-test guidelines.

The most effective measure to avoid vertical transmission is the use of antiretrovirals. The use of combined antiretrovirals is generally recommended from the 14th week of gestation and the use of intravenous AZT at delivery.

Adequate care for infected pregnant women involves, in addition to treatment with antiretrovirals capable of making and / or maintaining the viral load undetectable, general measures in prenatal care (such as care for the pregnant flora of the pregnant woman, vaccines), care during work delivery and suspension of breastfeeding.

Thus, the expansion of the offer of antenatal care and the improvement of its quality are essential conditions for the reduction of vertical transmission to effectively occur.

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