
# PREGNANCY IN HIV POSITIVE WOMEN IN POLAND. REVIEW OF EPIDEMIOLOGICAL SITUATION AND PATIENTS' MANAGEMENT

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## ABSTRACT

During pregnancy, various infections may be transmitted from the mother to the foetus, both through the placenta, during delivery and breastfeeding. In prevention of vertical transmission of infections, appropriate prophylaxis is important. HIV is a significant threat to both the mother and the foetus. It involves the risk of vertical transmission of the virus and the development of AIDS in both the mother and the child. In this review current reports from the field of gynaecology and infectious diseases regarding appropriate vertical transmission prevention in HIV positive pregnant patients are presented. The most important aspects of management of those patients were analysed and summarized. The risk of HIV transmission from the mother to the child without the implementation of appropriate prevention is 65-75%, but with appropriate care it is possible to reduce this risk to < 0.5%. HIV testing during pregnancy is an important element in the prevention of infections. The fastest possible implementation of treatment in HIV positive pregnant patients and prophylaxis in a child born by a HIV positive mother, significantly reduces the risk of transmission of the virus from the mother to the child.

## BACKGROUND

The period of pregnancy is divided into three trimesters, the first trimester lasts from 1 to 14 weeks of pregnancy, the second trimester from 15 to 28 weeks of pregnancy, and the third trimester from 29 to 42 weeks of pregnancy, respectively. It is important to exclude the most serious infectious diseases both for the mother and the foetus during pregnancy by means of appropriate tests. Among the infectious diseases for which the patients are routinely examined during the first trimester of pregnancy are syphilis, HCV, HIV, toxoplasmosis and rubella, in the second trimester tests for toxoplasmosis are repeated if the previous test was negative, while in the third trimester pregnant patients are tested towards HBV, HIV, colonization of GBS and towards HCV and syphilis in patients with an increased population risk or an individual risk of infection [1]. After a natural physiological childbirth, the newborn is not washed, skin contact should be ensured with the mother's skin and breastfeeding should be initiated. Newborns are vaccinated against Hepatitis B and tuberculosis (BCG) in the 1st day of life if there are no contraindications (e.g. low birth weight <2000g) [2].

In the beginning of the epidemic, HIV infection was a fatal sentence, but now it is considered as a chronic disease, the course of which can be significantly slowed down by implementing appropriate treatment through the selection of appropriate drugs. According to the National Institute of Public Health - National Institute of Hygiene (NIPH-NIH) in Poland between 1985 and 2018, HIV infection was diagnosed in 23311 people. In statistical practice of the Central Statistical Office, a reproductive age for the temperate climate zone, in which Poland is located, is 15-49 years [3]. There were 9 065 613 women of childbearing age in Poland in 2017 [3]. According to NIPH-NIH, the number of registered HIV-infected women of childbearing age reached 152 [4].

There are three stages of HIV infection [5]. First stage is acute HIV infection which develops within 2 to 4 weeks after exposure to HIV. In the acute stage of infection, the virus multiplies rapidly and spreads throughout the body. It attacks and destroys the infection-fighting CD4 cells of the immune system. The second stage of HIV infection is chronic HIV infection. During this stage of the disease, HIV continues to multiply in the body but at very low rates. People with chronic HIV infection may not have any HIV-related symptoms, but they can still spread HIV to others. AIDS is the final, most severe stage of HIV infection. HIV-infected patients are diagnosed with AIDS, if they have a CD4 count of less than 200 cells/mm3 or if they have certain opportunistic infections [6]. Without treatment, people with AIDS typically survive about 3 years [6].

Every pregnant woman should be offered a test for HIV during the first prenatal visit [7]. If the test is negative in the first trimester, it should be repeated in the third trimester. In the case of patient's refusal to perform the test, such information should be noted in medical records and patient should be treated as an infected person [7]. In pregnant women who begin prenatal care after the 20th week of pregnancy, such test should be performed urgently or a rapid test should be used after informed consent [7]. If pregnancy infection is confirmed, multidisciplinary specialist care is required during pregnancy and delivery, provided by the obstetrician, the infectious disease specialist dealing with the therapy of HIV positive patients, the neonatologist and the paediatrician. In case of women who are addicted to psychoactive substances, the psychiatrist must join the team [7].

## MATERIAL AND METHODS

In this review current reports from the field of gynaecology and infectious diseases regarding prevention of vertical transmission in HIV positive pregnant patients are presented. The most important aspects of management of those patients were analysed and summarized.

## DISCUSSION

During the pregnancy in a HIV positive patient, it is important to remember, that undetectable viremia is present. Especially during labour, this viremia increases the risk of transmission up to 65-75% [8]. Factors important for transmission of mother-to-foetus virus include: the lack of or ineffective antiretroviral treatment during pregnancy, maternal viremia over 100 000 copies/ml, premature rupture of membranes, foetal exposure to blood and maternal secretions, amniotic fluid with blood sucked out of the respiratory tract, preterm delivery < $37^{th}$ gestational week or post-term > $40^{th}$ gestational week, foetal outflow > 4h for viremia in a woman > 50 copies/ml, forceps delivery, perineal incision, vaginal birth with viremia > 1000 copies/ml, chorioamnionitis, child exposure after delivery through breastfeeding, the child's exposure during caesarean section, e.g. through cuts [8].

Due to the specific barrier made by the placenta, the risk of intrauterine virus transmission is much lower and amounts to 5-10% [8]. However, in untreated patients, the chance of infant's infection during breastfeeding is 10%, and the risk may increase up to 40% if the feeding period exceeds 6 months [8].

The achievement of undetectable viremia, at least in the third trimester, especially during labour, reduces the risk of vertical infection to <0.5% [8]. Each patient should be examined for drug resistance before starting treatment and in the case of ineffective therapy, depending on the situation, various therapeutic options should be considered [8].

Every pregnant HIV positive patient should be monitored for the potential side effects of antiretroviral treatment (anaemia, elevated aminotransferase activity, acidosis, hyperglycaemia) once a month and as often as possible during the anticipated labour the viremia and CD4 lymphocytes level [8].

A woman who plans to become pregnant and is already on ART therapy should continue it, provided she does not receive any drugs contraindicated during pregnancy. A pregnant woman who has not been treated with ART should start the therapy immediately [8].

A woman who begins obstetric observation in the second or third trimester should also start ART as soon as possible and consider adding integrase inhibitors (INSTI)

in order to rapidly reduce viral load and ensure that HIV RNA is absent during the delivery [8]. In turn, a pregnant woman with detectable viremia in the third trimester should undergo a drug resistance test and consider changing the treatment to an INSTI or adding if not receiving a drug from this group to reduce HIV RNA as soon as possible [8].

Among the anti-retroviral drugs used in pregnancy, RAL, DTV, RPV or DRV can be continued, if they were used before pregnancy. Women taking EVG/c should be informed that the level of HIV RNA should be controlled more frequently [8]. Among the protease inhibitors, ATV is preferred. EVF is an alternative for beginning treatment during pregnancy and it can be continued if it had been administered before pregnancy. NVP is not recommended for initiating treatment during pregnancy, but it can be continued, if it had been introduced earlier [8]. Therapy schemes contraindicated in pregnancy include: ddI + d4T and combinations of three NRTIs [8].

Natural childbirth in a woman infected with HIV is recommended when pregnant during pregnancy received ART and has undetectable HIV viral load < 50 copies/ml. Any non-standard situations during delivery such as induction of labour due to obstetric reasons, drainage of amniotic fluid > 4 hours, preterm delivery are not indications for administration of ZDV during delivery, but are indications for wider post-exposure prophylaxis of the newborn. Recommendations for caesarean section for obstetricians in women with HIV viral load < 50 copies/ml are the same as for women who are not HIV positive. Planned caesarean section at 38 weeks of gestation should be performed if HIV viral load before delivery in week 34-36 is detectable > 50 copies/ml or is unknown. A pregnant woman who was diagnosed with HIV very late or during the delivery period should be treated as a patient with high viral load and a caesarean section should be performed [8].

The newborn of the HIV positive mother should be washed immediately, rubbed off, have aspirated content from the upper respiratory tract, given antiretroviral medication within 4 hours after delivery and not later than 48 hours of life (therapy must last 4 weeks). Breastfeeding is contraindicated. In terms of vaccination, only the vaccine against hepatitis B is administered in the first day of life. BCG vaccination is postponed, it can be performed only after excluding a vertical infection in a child about 4-6 months old [9].

Dosage of zidovudine depends on the week of pregnancy and the risk of transmission of the virus from the mother to the child [9].

Newborns from the low risk group of HIV vertical transmission (mothers with HIV VL < 50 copies/ml and no additional risk factors at labour) born after 35$^{th}$ gestational week are administered for 4 weeks 4 mg/kg every 12 h orally or 3 mg/kg every 12 hours intravenously [9]. Premature infants between 30$^{th}$-35$^{th}$ gestational week are given 2 mg/kg orally every 12 hours for 2 weeks, then 3 mg/kg orally every 12 h for the next 2 weeks. In case of intravenous zidovudine treatment, this group of premature babies is given 1.5 mg/kg every 12 h for 2 weeks and 2.3 mg/kg every 12 h for the next 2 weeks. Premature babies born before 30$^{th}$ gestational week receive 1.5 mg/kg every 12 hours intravenously or 2 mg/kg every 12 hours orally for 4 weeks [9].

Newborns from the high-risk group (mothers with HIV VL > 50 copies/ml and < 1000 copies/ml) should be given ZDV according to neonatal doses and 3 oral doses of NVP 8 mg for newborns weighing 1.5- 2 kg and 12 mg for newborns of more than 2 kg, respectively, within 48 hours of life, 48 hours from the first dose and 96 hours from the second dose [9].

Newborns from the high-risk group (mothers with HIV VL > 1000 copies/ml) born after 32$^{nd}$ gestational week are advised to be given three drugs: ZDV in a dose as above, 3TC 2 mg/kg every 12 hours for 4 weeks and NVP 2 mg/kg every 24 hours for the first 7 days of life, then every 12 hours for the next 7 days. Premature babies born between 30$^{th}$-32$^{nd}$ gestational week are treated with 4-week ZDV and NVP in a dose as in high-risk children. In premature babies less born before 30$^{th}$ gestational week, regardless of the risk of virus transmission, only ZDV is used for 4 weeks [9].

## CONCLUSION

HIV testing during pregnancy is an important element of infection prevention. The fastest possible implementation of treatment in HIV positive pregnant patients and prophylaxis in the child of the HIV positive mother significantly reduces the risk of transmission of the virus from the mother to the child.

## CITE THIS AS

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## ABBREVIATIONS

**ART** – antiretroviral therapy
**ATV** – Atazanavir
**ddI** – Didadosine
**DRV** – Darunavir
**INSTI** – integrase inhibitors
**NIPH-NIH** – National Institute of Public Health - National Institute of Hygiene
**NRTIs** – Nucleoside reverse transcriptase inhibitors
**NVP** – Nevirapine
**RAL** – Raltegravir
**RPV** – Rilpvirine
**d4T** – Stavudine
**ZDV** – Zidovudine

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