

Epidemiology, etiology, pathogenesis and risk factors of mother-to-child-transmission of HIV

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Abstract

Two million children are estimated to be infected with HIV worldwide. Globally, every day 9 thousand people die of AIDS and 16 thousand become infected with HIV, including around 10% of children. In the latter group, the most frequent manner of HIV infection involves maternal transmission. In Poland around 15 thousand cases of HIV infection have been already noted, including around 150 children. In Poland, every year around 70 to 100 deliveries are by HIV-infected mothers. The vertical transmission may take place inside uterus (25-35% cases), during delivery (70-75%) or after birth, during breast-feeding (10-16%). The most important risk factors for HIV vertical transmission include high HIV load in a mother, improperly conducted prenatal antiretroviral therapy and concurrence of other sexually transmitted diseases.

Key words: epidemiology, etiology, HIV infection, HIV-MTCT.

Epidemiology of HIV infection

Worldwide situation

Most probably over two million HIV-infected children live in the world [1]. It is estimated that every day 9 thousand persons die of AIDS and 16 thousand become HIV-infected, of whom around 50% involve persons aged 15-24 years and 10% are children [2]. The number of new HIV infections in the world's population decreases. In 2009, globally around 2.6 million infections were noted or 19% less than in 1999. The region most affected by the infections is the Sub-Saharan Africa, with the majority of new infections, although even there a decreasing tendency is noted (2001 – around 2.2 million, 2009 – 1.8 million). This reflects both efforts of several international organizations and state governments and the natural course of AIDS epidemics [3]. The worldwide increased accessibility of prophylaxis against vertical infections resulted in a decrease in the number of HIV-infected newborns. In 2009, around 370 thousand of such children were delivered in the world or by 24% less than in 2004 [3]. More than 1000 children daily are estimated to be infected with the virus, first of all in the Third World countries [4]. In the case of HIV-2 virus, the infection is very infrequently trans-

mitted from the mother to her child (risk of MTCT: 0-4%) [5, 6]. Moreover, manifestation of HIV-2 is of an endemic type (West Africa, foci in India, Portugal) [7]. Progression of HIV-2 infection toward AIDS is much slower [8]. In developed countries, the risk of vertical infection is much lower. In the pre-HAART era, it was 25%. At present, in the USA it amounts to less than 2%, [9], and in Japan – 0.45% [10]. Annually, less than 200 vertical infections with HIV develop in the United States [11-13].

Situation in Poland and the Middle-Eastern Europe

Statistically, every day one or two Poles learn that they are infected with HIV [2]. According to the National Institute of Hygiene (NIH), 14,725 Polish citizens became HIV-infected between 1985 and 31 July 2011. 17.8% of them developed AIDS and, till now, 1103 Polish citizens have died of AIDS [14]. However, it remains very difficult to keep a reliable statistic of newly detected infections with HIV since NIH receives no data about cause of infection. In July 2011, in as many as 66.7% reports no most probable cause of the infection was given [14]. Currently, around 10 thousand of HIV-infected persons live in Poland and, until now, 147 infections have been detected in children [15]. The National AIDS Centre announced that in mid-August 2011, over 5401 patients were receiving antiretroviral treatment

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in Poland, including 136 children. Annually, in Poland around 70 to 100 HIV(+) mothers deliver babies. It remains disturbing that it happens that HIV infection of a mother becomes established after detection of the virus in a newborn/child. The promotional campaign entitled "Give a chance to your kid, do not give a chance to AIDS" launched in 2007 and renewed in 2009, aims at changing this state of affairs [16]. In Poland, over half of HIV-infected persons do not know that they carry the virus [15] (Figure 1).

In the Western, Middle and Eastern Europe the number of new cases of HIV infection is stable [3]. In Ukraine, which neighbors Poland, in which 1% of the society is infected with HIV, the number of new cases decreases as a result of respective preventive activities introduced [3, 17, 18].

Etiopathogenesis and risk factors for HIV vertical transmission

Vertical infection (MTCT) represents the most common cause of infection in childhood. It may occur in three periods, including intrauterine infection, infection during delivery or during breast-feeding [19]. Currently, infection with HIV due to blood transfusion is thought to be practically impossible. Nevertheless, the infection mediated with blood remains a statistically significant cause of infections in individuals using intravenous stupefying agents [2]. In untreated HIV-infected pregnant women, the risk of transmission is 19-36%. Out of all infections, 25% to 35% of infections develop during pregnancy, mainly in late in pregnancy, 70% to 75% during delivery and 10% to 16% during breast-feeding [20]. The most significant risk factors for viral infection to the fetus include high viral load in the mother's blood and improper antiretroviral therapy (ART) [21]. Failure to perform a planned cesarean section remains to be a statistically significant risk factor [22, 23]. An increased probability of MTCT results also from presence of other sexually transmitted diseases, progressive accompanying diseases as well as all situations which increase probability of contact between fetus/newborn blood and mother's blood [1]. Infections with pathogens such as *Herpes simplex*, *Treponema pallidum*, *Haemophilus ducreyi*, the most important causes of ulceration in genital organs, may result in a 100-fold higher probability of HIV transmission. This is linked to mechanical damage of mucosa or epidermis and the inflammatory process [24-26]. Inflow of macrophages and lymphocytes T to sites exposed to virus transmission increases the risk of transmission since the virus manifests the highest affinity to intraepithelial CD4+ cells and to Langerhans cells of vagina [27].

Preterm newborns are more prone to become infected with HIV [28]. A higher MTCT risk was noted in pregnant women using illegal stupefying substances. This was so because, first, such mothers less frequently followed medical recommendations and, second, opioids promote

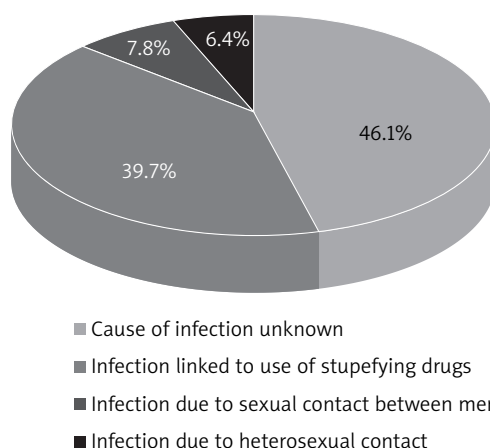


Fig. 1. Causes of HIV infection in Poland in 1985 to 31st January, in %. Prepared on the basis of NIH database

penetration of HIV to macrophages [21]. Studies performed in Africa indicate that vitamin A supplementation during pregnancy and thereafter exerts a negligible, if any, effect on MTCT [4]. In the USA, despite the satisfactory access to ARV drugs, perinatal infections with HIV still do occur. The phenomenon reflects mainly the continuous increase in the proportion of women at the reproductive age in the HIV-infected population, absent or exceedingly late prenatal care, particularly in a group of mothers using illegal stupefying agents, primary HIV infection in late pregnancy or during breast-feeding, failure to follow medical recommendations related to ARV therapy as well as failure to undergo a routine prenatal examination and medical consultations [13, 29]. In a group of untreated HIV infected newborns in around 20% of cases, a rapid progression follows to AIDS within the first year of life [30]. In children, treatment and diagnosis of HIV infection pose more difficulties than in adults [31], although early diagnosis followed by an appropriate treatment highly increase the probability of survival for the child [32]. Therefore, prophylaxis against vertically transmitted infections and early application of ART in the case of newborns whose mothers have not been covered by prophylaxis seem to be immensely important.

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Appendix

Definitions, legend of acronyms

AIDS – acquired immunodeficiency syndrome, resulting from HIV infection and diagnosed when the patient begins to manifest index diseases of AIDS and/or when the number of CD4(+) cells in blood amounts to < 200 CD4+ cells/ μ l [2]

ARV – antiretroviral

ART – antiretroviral therapy [7]

cART – combination antiretroviral therapy consisting of antiretroviral drugs originating from various therapeutic groups.

European definition of HIV/AIDS – laboratory criteria. In children below 18 months of life, the diagnosis is established by positive results in two independent samples (not of umbilical blood) obtained in the following tests: tests aimed at isolation of HIV; tests for presence of viral nucleic acids (HIV-RNA, HIV-DNA); tests for presence of p24 antigen, including virus neutralization test in a child in the first month of life [33]. In children above 18 months of life, in youth and adults (i.e. in individuals older than 13 years of age), AIDS is diagnosed when at least one of the following conditions is met: 1) a positive result of a screening test for presence of HIV-specific antibodies or a test for presence of antibodies and p24 antigen, confirmed by a more sensitive test, e.g. Western Blot; 2) positive results of two immunoenzymatic (EIA) tests, confirmed by positive results of the third identical test; 3) positive results for two separate samples in at least one of the following tests: detection of nucleic acid (HIV-RNA, HIV-DNA); test for presence of p24 antigen, including the neutralization test; isolation of HIV [34]. According to the European definition, HIV infection is diagnosed in every person who meets respective laboratory criteria while AIDS is diagnosed in every individual who meets clinical criteria of AIDS and laboratory criteria of HIV infection

HAART – highly active antiretroviral therapy consisting of three or more antiretroviral chemotherapeutic drugs. Schemes, which used to be suggested, consisted of two RTIs and one PI or three RTIs [35]. Although no single perfect HAART scheme is available, clinical trials indicate that PI-containing schemes significantly improve quality of life and nutritional status of patients [36]. It is worth stressing that application of HAART, which exerts toxic effects on mitochondria, brings about multiple undesirable effects, starting from variably intense hypersensitivity reactions, gastrointestinal problems, metabolic disturbances (hyperinsulinemia, hyperlipidemia, insulin resistance, etc.), lipodystrophy, to hepatotoxicity, pancreatitis or even toxic effects on the central nervous system and many other [37, 38]

HIV – human immunodeficiency virus. It belongs to retroviruses. In most of cases, the infection involves the

HIV-1 virus [1]. HIV-2 is manifested endemically and, what is significant, it does not respond to NNRTI treatment due to differences in the structure of reverse transcriptase [39]

MTCT – mother-to-child transmission (of HIV) – vertical infection (transmission) of HIV from the mother to the child which may be intrauterine, perinatal or through breast-feeding [21]

NNRTI – non-nucleoside reverse transcriptase inhibitors; e.g. nevirapine, efavirenz [40]

NRTI – nucleoside reverse transcriptase inhibitors, including zidovudine, lamivudine, abacavir, emtricitabine, etc.

PI – protease inhibitors that inhibit production of normal viral proteins, which blocks formation of virions and viral replication (e.g. ritonavir, saquinavir)

PMTCT – preventing mother-to-child transmission (of HIV) – a set of medical activities aimed at preventing transmission of HIV from the mother to her child, which is not finished upon delivery but assumes subsequent activities performed both in the mother and in the child

RTI – reverse transcriptase inhibitors. This group of drugs encompasses nucleotide analogs (e.g. tenofovir) and, as explained below, nucleoside analogs and non-nucleoside analogs [7]