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CLINICAL STUDY

HIV prevalence and clinical care for HIV-positive pregnant women in Slovakia

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Abstract: *Objective:* To evaluate clinical care for HIV positive pregnant women who delivered in Slovakia from 1985 till 2008.
Background: National guidelines for the prevention of mother-to-child transmission of HIV have not yet been established.
Method: Retrospective analysis of 14 HIV-infected pregnant women and their infants. Factors examined include maternal social, demographic, immunological and virological characteristics, method of HIV testing, antiretroviral therapy during pregnancy, delivery and puerperium, mode of delivery, mode of infant feeding, pregnancy outcomes and HIV status of infants.
Conclusions: Due to the increase in cases of HIV-infected pregnant women within the last several years, it would be advisable to create National Guidelines for PMTCT (Prevention of Mother-to-Child Transmission) in order to consolidate the care management in all HIV/AIDS care centers around Slovakia *(Fig. 4, Ref. 7)*. Full Text (Free, PDF) *www.bmj.sk.*
Key words: HIV, vertical transmission, prevention, pregnant women.

Vertical transmission of the human immunodeficiency virus (HIV) is the main source of HIV infection in children throughout the world. It is estimated that 2000 vertically acquired HIV infections occur daily worldwide (1). The advances in antiretroviral prophylaxis and management of pregnancy, delivery and puerperium have achieved a dramatic reduction in vertical transmission rates. Where these effective interventions are freely available and used, mother-to-child transmission rates of 1–2 % are achievable (1, 2, 3).

In Slovakia, HIV testing was first established in 1985 (4). However, the first delivery of HIV-infected woman did not occur until 1997. Since then a gradual increase in cases of HIV-infected pregnant women who gave birth can be seen. Figure 1 shows the number of deliveries of HIV-infected pregnant women from 1997 till 2008 (Fig. 1).

By 31st of December 2007, 4 321 436 blood samples were tested for HIV. Out of these, 323 samples were confirmed HIV positive. 69 % (n=224) of positive cases were Slovakian citizens and 31 % (n=99) were foreigners. Out of 224 Slovakian citizens, 80 % (n=180) were males and 20 % (n=44) females. Male and female ratio was 4 : 1. In 89 % (n=39) of Slovakian women, heterosexual acquisition was described. In 4 % (n=2), intravenous drug use as a mode of HIV transmission was described and in 7 % (n=3), the mode of HIV transmission was not known or not described (5). Figure 2 describes an increase in cases of

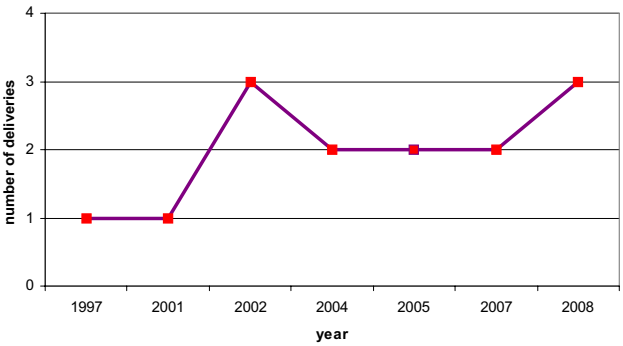

Fig. 1. Number of deliveries of HIV positive women in Slovakia from 1997 till 2008.

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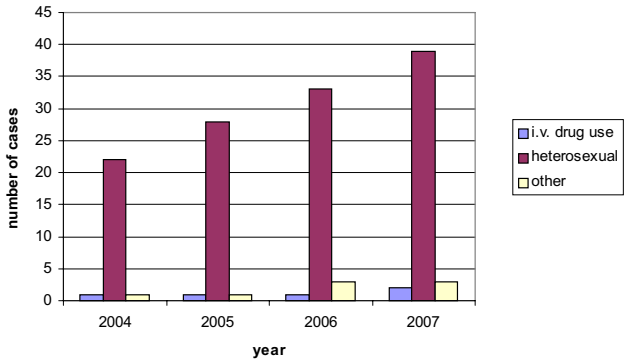

Fig. 2. The mode of HIV transmission among Slovakian women from 2004 till 2007.

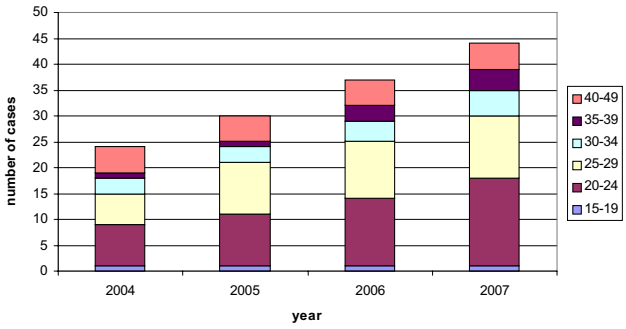

Fig. 3. Number of HIV positive women devided into age groups.

HIV-positive women infected by heterosexual acquisition within the period from 31st of December 2004 till 31st of December 2007.

Among the 44 HIV-positive Slovakian women, 89 % (n=39) were of the reproductive age (15–39 years). 11 % (n=5) were among the age group of 40–49 years (5). The numbers of HIV-positive women changing over a period of 4 years (31st of December 2004 till 31st of December 2007) are shown per different age groups in Figure 3.

Pregnant women in Slovakia are tested voluntarily in their first trimester of pregnancy and repeatedly in the third trimester. Mandatory testing of pregnant women was enforced by law within a period of one year from 1991 till 1992. No pregnant woman was found HIV positive during this period of mandatory testing (4).

Method

Analysis of retrospective data on 14 HIV-infected pregnant women and their infants. Medical files were reviewed and data collected from all three HIV/AIDS care centers around Slovakia in the cities of Bratislava, Banská Bystrica and Košice. The examined factors included maternal social, demographic, immunological and virological characteristics, method of HIV testing, antiretroviral therapy during pregnancy, delivery and puerperium, mode of delivery, mode of infant feeding, pregnancy outcomes and the HIV status of infants.

Results

Maternal social, demographic and HIV-related characteristics

Method of HIV testing and time of comfirmed HIV-positive results: By August 2008, 14 HIV-infected women delivered in Slovakia. HIV screening was performed using ELISA (Enzyme Linked Immunosorbent Assay) for anti-HIV 1/2 and detection of antigen p 24. All of the reactive samples were retested and confirmed positive by Western blot at the National Reference Center for HIV/AIDS in Bratislava, where all of the positive results from Slovakia are registered. 79 % (n=11) of these women were diagnosed as HIV-infected prior to pregnancy, in 7 % (n=1), HIV infection was diagnosed during pregnancy, and the remaining 14 % (n=2) were diagnosed after the delivery.

Age: The median of maternal age at the time of delivery was 28 years with a minimum of 22 and a maximum of 38 years.

Parity: 14 % (n=2) of HIV-infected women gave birth for the first time. 36 % (n=5) gave birth for the second time and in the remaining 50 % (n=7) the information about parity was not included in medical files.

Marrital status: 64 % (n=9) of women were married, 7 % (n=1) single, 7 % (n=1) divorced, and in 22 % of cases (n=3), the information about marital status was not included in medical files.

Partner's HIV status: in 43 % (n=6), the information about HIV testing was not stated in medical files. Out of the remaining 57 % (n=8) with known HIV status, 6 partners were confirmed HIV negative and 2 HIV positive.

Immunological status: immunological status was defined depending on CD4 cell count evaluated in the last blood sample drawn prior to delivery. Information on CD4 cell count was available for 13 (93 %) mothers, with a median of 428.5/mm^3 (106–834/mm^3).

Virological status: virological status was defined by viral load (number of HIV RNA copies per 1 ml of blood) evaluated in the last blood sample drawn prior to delivery. The information on viral load was available for 12 women (86 %), and for 2 women (14 %) the information was not available.

Out of all women with known viral load, 42 % (n=5) had undetectable levels of virus defined as <400 copies/ml. In 8 % (n=1), the viral load was <1000 copies/ml (831 copies/ml) and in 50 % (n=6) of women, the viral load was >1000 copies /ml (1 490–24 300 copies/ml). Among the tested women with viral load >400 RNA copies/ml, the average viral load was 6 054 HIV RNA copies/ml.

Coinfection with other sexualy transmitted infections: Serological test for hepatitis B virus (HBV) by detection of HBsAg and lues testing (TPHA a RPR) was performed and the results were available in 71 % (n=10) of mothers. All of them were confirmed to be HBsAg and lues negative. In 29 % (n=4), no

information about HBsAg and lues testing was available. Testing for hepatitis C (HCV) and results of the tests were available in all 14 mothers. In 29 % (n=4), HCV coinfection was confirmed. In the remaining 71 % (n=10), the result for HCV testing was negative. In 2 women, hepatitis C coinfection was confirmed during pregnancy. In 50 % (n=2) of women with HIV/HCV coinfection, the history of intravenous drug use was stated.

Antiretroviral prevention of vertical transmission of HIV

National guidelines for the prevention of vertical transmission of HIV have not yet been established. Therefore, there are no recommendations for the use of specific antiretrovirals, appropriate dosing and indications of use for the prevention of mother-to-child transmission of HIV in Slovakia. Infectologists specialised in the care for HIV-infected patients are responsible for the management of antiretrovirals during pregnancy, delivery, and after delivery for mother and for antiretroviral post-exposure prophylaxis in their infants. Appropriate antiretrovirals used in HIV-infected pregnant women were chosen depending on clinical symptoms, virological and immunological status of the woman, and the results of antiretroviral drug resistance testing.

Differences in the management of antiretroviral therapies among HIV positive pregnant women who delivered at different HIV/AIDS care centers in Slovakia were observed.

Antiretrovirals predominantly used during pregnancy: HIV-infected pregnant women who do not require antiretroviral treatment for their own health due to their good immunological and virological status are in order to reduce the risk of vertical transmission of HIV started on a combination of antiretrovirals as follows:

– Ziduovudin (AZT) 300 mg + Lamivudin (3TC) 150 mg

This combination of antiretrovirals is started at the beginning of 2nd trimester of pregnancy and is used twice daily throughout the pregnancy.

HIV-infected pregnant women who require antiretroviral treatment for their own health due to their high immunological deficit and viral load or due to their clinical status are started on appropriate combination of three or more antiretrovirals called HAART (Highly Active Antiretroviral Therapy). The most appropriate antiretrovirals used for treatment are chosen in accordance with information on their possible teratogenic effects on fetus, and other factors like coinfection of the woman with HCV or HBV, resistance of HIV to certain antiretrovirals and depending on other possible side effects of these medications. Each woman has to be completely assessed and the most appropriate combination of antiretrovirals is chosen for each case in accordance with these factors.

Antiretrovirals used during delivery: In general, Zidovudin (Retrovir™) is used during delivery as an intravenous infusion in a dose of 200–400 mg depending on the weight of the HIV-infected woman. Infusion is started up to 4 hours prior to scheduled caesarean delivery and continued until the umbilical cord is clamped.

Out of all 14 HIV-infected women who gave birth, 71 % (n=10) received Zidovudin infusion (RetrovirTM). 14.5 % (n=2) women had not received any antiretrovirals during delivery as their HIV status was confirmed after the delivery, and in 14.5 % (n=2), the information on use of antiretrovirals during delivery was not stated in their medical files.

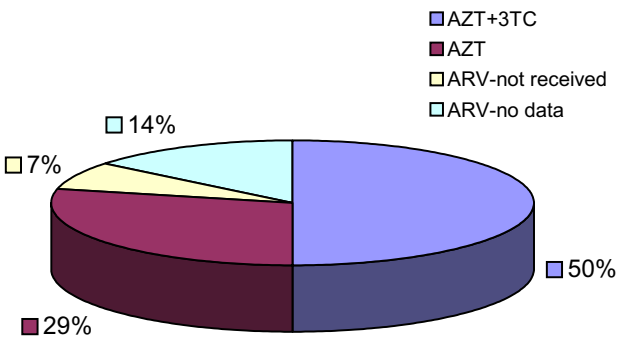

Fig. 4. Newborns devided into groups depending on the antiretrovirals used.

Antiretrovirals used for post-exposure prophylaxis of the newborn of HIV-infected women: The newborns of HIV-infected women who delivered in Slovakia were given one of the following antiretrovirals:

a) Zidovudin solution, in a dose of 2 mg/kg every 6 hours,

b) Zidovudin solution, 2 mg/kg every 6 hours + Lamivudin solution 4 mg/kg every 12 hours.

The newborns were started on one of the latter medications within few hours after delivery and continued for a period of 4 weeks.

All 14 newborns can be divided into groups depending on the used antiretroviral regime as follows:

Group 1 — 50 % (n=7) newborns received a combination of AZT solution (2 mg/kg) + 3TC solution (4 mg/kg) (in accordance with scheme a) 6 of these were born at the HIV/AIDS center in the city of Bratislava and 1 in the city of Banská Bystrica.

Group 2 – 29 % (n=4) newborns received only the AZT solution (2 mg/kg) All of them were born at the HIV/AIDS Center in the city of Košice.

Group 3 – 7 % (n=1) had not received any antiretrovirals, as the HIV status of their mother was confirmed after the period of 4 weeks after delivery, during which the newborns are usually on this treatment.

Group 4 – 14 % (n=2) did not have any information on antiretrovirals used.

The division of all of the newborns divided into the groups in accordance with the antiretroviral regime used are shown in percentage in Figure 4.

Mode of delivery

In all HIV-infected women whose HIV status had been known prior to delivery, elective caesarean section was scheduled. However, 14 % (n=2) of women delivered vaginally without the use of any appropriate preventive measures of reducing the risk of mother-to-child transmission of HIV since their HIV status had

not been known prior to delivery and there had not been other indications for caesarean delivery. In the remaining 86 % (n=12), elective caesarean section was performed prior to the rupture of the membranes. All of these were performed in one of the HIV/AIDS Centers: 50 % (n=6) in Bratislava, 8 % (n=1) in Banská Bystrica and 42 % (n=5) in Košice.

Antibiotic prophylaxis used during delivery and early puerperium

In 64 % (n=9) of cases, antibiotic prophylaxis was used during delivery and continued in puerperium. In 67 % (n=6), cefalosporines were used, and in the remaining 33 % (n=3), antibiotics from the penicillin group were used. All of them were started intravenously and some were followed by oral administration for up to 7 days. In 22 % (n=3), no antibiotics were used in order to prevent the infectious complications associated with operative delivery (caesarean section). The remaining 14 % (n=2) had not received any antibiotics during the delivery or puerperium, as their HIV status was confirmed only after the delivery.

In the 14 HIV-infected women who gave birth, no complications in form of puerperal infection were observed.

General characteristics of the newborns group and their clinical status after birth

None of the newborns came from a multiple pregnacy, therefore 14 newborns were born in Slovakia up to August of 2008.

Gender: 50 % (n=7) were males, 43 % (n=6) females and in 7 % (n=1), the information about gender of the newborn was not available.

Weight: The average neonatal weight of the newborns was 3 100 grams. The average weight in the female group was 3 305 grams (2,850–4,500 g). The average weight in the male group of newborns was 3,120 grams (2,680–3,510g) while a male newborn born prematurely and with symptoms of hypotrophy with neonatal weight of 1,750 grams was not included in the average weight count.

Length: *The m*edian of neonatal length in the group of 13 newborns with available data was 50 cm.

Clinical status: The clinical status defined by APGAR score in the 1st and 5th minutes of life was available for all 14 newborns of the group. The median of APGAR score was 9/10.

Congenital abnormalities: No congenital abnormalities were observed in any of the 14 newborns of HIV-infected mothers.

Infant feeding

Out of all newborns (n=14), 86 % (n=12) were formula fed, 7 % (n=1) had been breastfed as the HIV status of their mothers was confirmed only after puerperium, and in 7 % (n=1), no information about the mode of their feeding was available as the medical file of the newborn was missing.

Method of HIV testing of infants and vertical transmission of HIV

Infants of HIV-infected mothers are subsequently under simultaneous testing using serological (ELISA) and moleculo-biological (PCR) methods for the period of 2 years. In general, 5 tests are performed at the age of 3 and 6 months, and 1 at 1.5 and 2 years of age.

All of the infants' blood samples tested for HIV by the end of 2008 were confirmed HIV negative.

Discussion

Observational data indicate that among the Slovakian citizens, the number of HIV-infected women in the age group of 15–49 years has increased over a period of 4 years from 2004 till 2007. While in 2004, the number of HIV-infected women in the latter age group was 24 cases, in 2007 it was 44 cases. A similar increase in cases of HIV-infected women in the age group of 15–49 years was described in the female population of the European Union (6).

Also, the number of newly HIV-infected in the general population has been increasing in Slovakia since 1985. Similar increases in newly infected have been described in European Union cummulative data (6). In Slovakia in 1985 there was only one reported case of new HIV infection; in 2007, 39 cases of new infection were reported. This is equivalent to the incidence of 7.2 cases per one million inhabitants. This incidence of new cases of infection by 31st december 2007 is the lowest among all of the coutries of Europen Union. The 2007 incidence of newly acquired HIV infections in the European Union was 63.5 per million inhabitans (6).

The data describing the time of confirmation of HIV status, immunological and virological status, average age at the time of delivery and mode of delivery of all HIV-infected women who gave birth in Slovakia can be compared with those described in the European collaborative study. It was a prospective study conducted on 2,876 pregnant HIV-infected women and their 3,076 infants. It described changes over a 15-year period since 1986 (7).

No significant difference in the median CD4 cell count was observed between women who delivered in Slovakia and women included in the European collaborative study. The median CD4 count in this collaborative European study was 440/mm^3 (7), which was similar to the CD4 count of 428,5/mm^3 in the group of HIV-infected pregnant women who delivered in Slovakia up to august 2008.

The viral load data were available in 86 % of women from the Slovakian study. In the group of women evaluated in the European study, the information on viral load was available only in 14.5 % of cases (7). The average viral load in the Slovakian group was 6,054 RNA copies/ml. In the group of women in the European study, it was very similar at the value of 6,039 RNA copies/ml (7). 42 % of women from Slovakian group had a viral load <400 RNA copies/ml (undetectable), just as 42 % of women from the European study group (7). HIV infection was diagnosed before pregnancy in 48 % of women in the European study, while among women from the Slovakian study it was 79 % (7). While in Slovakia, 86 % of newborns were delivered by caesarean section, in the European study, only 10 % of pregnancies in 1992 were delivered by caesarean section, rising to 71 % in 1999/2000 (7).

Similar results were described in the average maternal age at the time of delivery. In Slovakia it was 28 years, while in the European study it was 27 years of age (7). In the European Union, there were 3,507 children who acquired HIV through vertical transmission as of December 2007 (6). This was the number of infected children after the reduction of risk of vertical transmission of HIV described in the European collaborative study with a documented decline from 15.5 % by end of 1994 to less than 2 % among mother-child pairs who completed the three component antiretroviral protocol, and there was no breastfeeding and elective caesarean section delivery performed (7). In Slovakia a 100 % succes rate in the prevention of mother-to-child transmission of HIV was achieved, i.e. HIV infection was confirmed in none of the newborns on subsequent testing after birth.

Conclusions

Despite the fact that no infant born in Slovakia of an HIV-infected woman was confirmed HIV positive, there is a need to create national guidelines for the prevention of mother-to-child transmission in order to maintain the favourable success rate in managing the risk of vertical transmission and to consolidate the care management in all 3 HIV/AIDS care centers around Slovakia. Since the medical files often lack the data on gynecological and obstetrical risk factors associated with HIV vertical transmission, it would be advisable to enhance the cooperation between infectologists and gynaecologogist/obstetritians. Creating a PMTCT summary sheet for guidance and identification of risks for vertical transmission of HIV should be considered.

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