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Epidemiological Study on Prevalence of HIV Infected Pregnant Women and Evaluation of Trans-Vaginal Delivery Regarding to Prevention of Mother-to-Child Transmission

Tsunekazu KITA, Naoto YOSHINO, Yuki TSUKAHARA, Masao TOGAWA, Noriyuki INABA and Yuichi WADA

Dept. Obstet. and Gynecol., Teikyo University School of Medicine and The National Cooperative Study Group on HIV Infected Pregnant Women and Mother-to-Child Transmission in Japan

Objectives:

In order to update the prevention methods of the mother-to-child transmission (MTCT) of HIV, we evaluated the clinical and virological information from HIV infected pregnant women and their off-springs in Japan. And then we identified the effectiveness of vaginal delivery to prevent MTCT of HIV comparing with elective cesarean section.

Methods:

For 10 years from 1998, a questionnaire about pregnant women infected with HIV was sent annually to more than 1,600 hospitals providing obstetric department and more than 3,500 hospitals or clinics providing pediatrics service. Totally 503 cases of HIV infected pregnancies were reported by 2007. Additionally, we obtained the details of the perinatal information of HIV infected 422 pregnant women from our obstetrics study group and 281 new born babies from pediatrics study group defined from 1987 to 2007 in Japan. After verification of these 703 cases, finally 503 cases by 2007 were evaluated in this study. Epidemioligical, obstetrical, and virological data on mothers and their infants was studied retrospectively.

Results:

Fig.1 shows the rate of pregnant women accepted voluntary HIV screening test in Japan. The screening rate of HIV infection was 95.3% in 2006 and elevated in 22.1% during the recent decade.

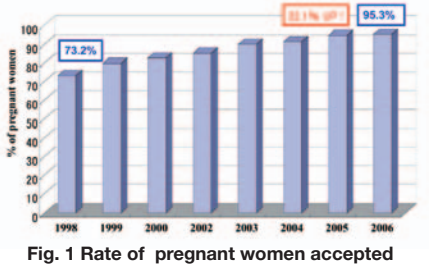

Fig. 1 Rate of pregnant women accepted voluntary HIV screening test in Japan

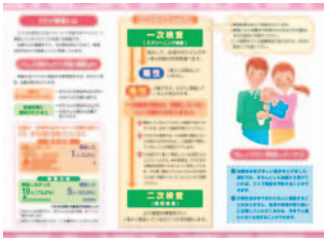

Fig. 2 Pamphlet informing HIV screening test for pregnant women

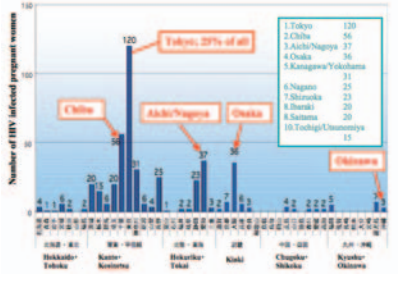

Fig. 3 Distribution of HIV infected pregnant women in provinces

These results are considered to be much indebted to publishing annual report and educational campaign by our study group. Fig.2 is a pamphlet informing HIV screening test for pregnant women established by our study group with supports of the Ministry of Health, Labour and Welfare in Japan.

The prevalence of HIV infected pregnant women is 9 per 100,000 pregnancies in Japan. Fig.3 shows distribution of HIV infected pregnant women in provinces and areas in Japan. About 65% of 503 cases from obstetrics and pediatrics study were

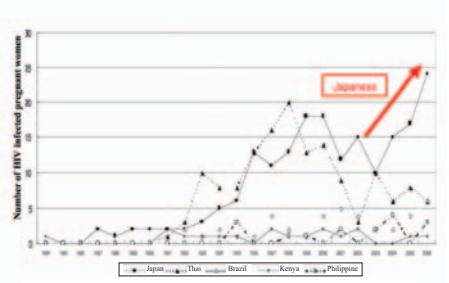

Fig. 4 Annual changes of number of HIV infected pregnant women in top 5 nationalities

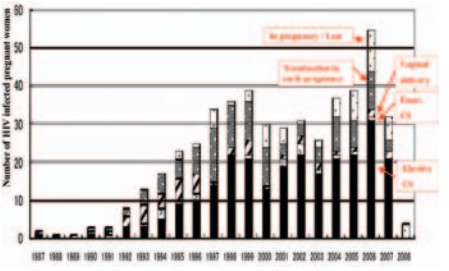

Fig. 5 Outcome of HIV infected pregnant women

reported in Kanto area around Tokyo metropolitan. One hundred and twenty cases, 25% of all cases were reported in Tokyo followed by 56 cases in Chiba, 37 cases in Aichi/Nagoya, 36 cases in Osaka and 31 cases in Kanagawa/Yokohama. On the other hand, only 3 cases were reported in Okinawa. Only few cases were reported in north-east and south-west areas in Japan.

Fig.4 shows annual changes of number of HIV infected pregnant women in top 5 nationalities. Japanese HIV infected pregnant women are increasing in this decade and taking the half of all cases. Brazilian is also increasing slowly in this decade. On the other hand, Thai is decreasing from 1999.

Annual outcome of HIV infected pregnant women was showed in Fig5. After 1997, 30 or more

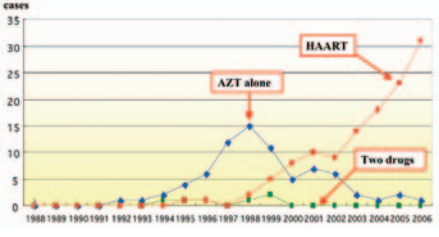

Fig. 6 Anti-retroviral therapy for HIV infected pregnant women

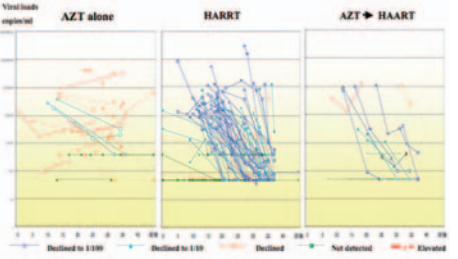

Fig. 7 Viral loads in HIV infected pregnant women treated with anti-retroviral drugs

cases were reported annually and misgivings of pandemic of HIV infected pregnant women should be considered. Out of 503 cases, 272 cases were resulted in elective cesarean section, 23 cases in emergency cesarean section and 60 cases in vaginal delivery. One hundred and three cases were terminated before 22 weeks of gestational age. Remaining 45 cases were during pregnancy or lost for follow up. About 90% of delivery cases chose elective cesarean section to prevent MTCT of HIV.

In Japan, HAART has to be standard regimen for HIV infected pregnant women from 2000. Fig.6 shows the number of cases of individual anti-retroviral therapy. Almost all patients were treated with HAART including AZT+3TC+NFV or AZT+3TC+LPV/RTV in recent years. Virus RNA levels were more than 100,000 copies/ml in 9.0% of cases, more than 10,000 copies/ml in 39.7% of cases and more than 1,000 copies/ml in 68.8% of cases from 244 cases measured. RNA viral loads declined to less than one per cent of the highest levels in 43.2% of cases and to less than one tenth in 73.9% of cases by HAART. On the other hand, RNA viral loads declined to less than one tenth of the highest level in only 16.1% of cases by zidovudine alone. The levels still more elevated during pregnancy in 19.4% of cases administered with zidovudine alone. Fig.7 shows viral loads in HIV infected pregnant women treated with anti-retroviral drugs. Viral loads have rapidly declined to 1/100 or under with HAART within 4 weeks. Meanwhile, viral loads declined slowly or elevated with AZT alone.

Table 1. Rate of mother-to-child transmission of HIV in delivery modes

Modes of delivery	Uninfected	Infected	Rate of MTCT	ART
Elective CS	193	1	0.5%	79.9%
Emergency CS	16	1	5.9%	52.9%
Vaginal delivery	19	5	28.8%	14.3%
Total	228	7	3.0%	

Table 2. Prevention of Mother-to-Child Transmission of HIV

1. Voluntary HIV screening test in early pregnancy
2. Anti-retroviral therapy with HAART in pregnancy
3. Elective cesarean section prior to the onset of labor
4. Zidovudine (AZT) d.i.v. during cesarean section for mother
5. AZT syrup for off-springs
6. Avoiding breastfeeding

Table 1 indicated the rate of MTCT of HIV in delivery modes. The rate of MTCT of HIV for elective cesarean section and vaginal delivery were 0.5% (1/194) and 20.8% (5/24), respectively. Anti-retroviral agents were administered for 79.9% of HIV infected pregnant women in elective cesarean section group and for only 14.3% of those in vaginal delivery group. Two mothers resulted in MTCT of HIV even after emergency or elective cesarean section took nothing or zidovudine alone before her delivery. Anti-retrovirus agents were never administered for any pregnant women resulted in MTCT after vaginal delivery.

There were only 8 cases reported in Japan who were diagnosed as HIV infection before their vaginal delivery. All cases could escape MTCT of HIV even if the reason of vaginal delivery was unclear. Three representative reports from Cochrane Database Syst Rev 2005, Clin Infect Dis 2005 and J Trop Pediat 2006 recommended differently for safe mode of delivery to prevent MTCT of HIV. Usefulness of elective cesarean section for HIV infected pregnant women well-controlled with HAART may still be unclear to prevent MTCT of HIV.

Table 2 shows the prevention methods of mother-to-child transmission of HIV recommended in Japan. Voluntary HIV screening test, anti-retroviral therapy with HAART in pregnancy and avoiding breast feeding are necessary for prevention of MTCT of HIV. However, these factors remain to be problems for countries providing insufficient test kits, anti-retroviral agents and milk for mothers. Although elective cesarean section seems to be commendable and is available in Japan because of sufficient medical cares and insurance supports, the mode of delivery should be recommended with informed consent after providing merits and demerits of the two modes of delivery for HIV infected pregnant women.

Fig.8 shows the guideline [Japanese] for prevention of MTCT in HIV infected pregnant women established by our study group with supports of the Ministry of Health, Labour and Welfare in Japan. This guideline is available from URL; http://api-net.jfap.or.jp/siryou.

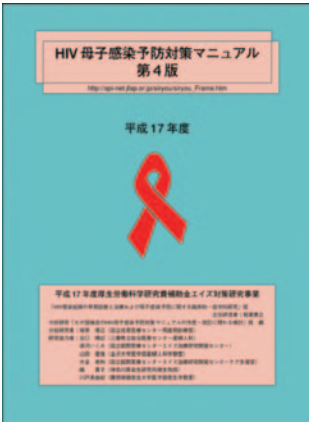

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Fig. 8 Guideline for prevention of mother-to-child transmission in HIV infected pregnant women (4th ed., 2006) URL; http://api-net.jfap.or.jp/siryou

Conclusion:

Japanese HIV infected pregnant women are increasing in recent years in Japan. MTCT rate was only 0.5% if conducted with anti-retrovirus agents and elective cesarean section. Viral load, the most important risk factor for MTCT of HIV, is not controlled enough by zudovudine alone. HAART is recommended to control viral load in HIV infected pregnant women. Combination of HIV screening, HAART and elective cesarean section is strongly recommended to prevent MTCT of HIV in Japan.

The above was excerpted from "Innovation of the Journal of AIDS Research 9: 6- 10, 116- 119 and 209-216, 2007".