J. of Obst. & Gyn. of India Vol. 51, No. 5 : September/October 2001 Pg 56-60

Perinatal Transmission of HIV Infection in Mumbai, India.

Deepti D. Dongaonkar, Anagha V. Jaykar, Subhash A Angadi, Clemente S Fernandes, Subhash K Hira, Naina Narkhede, Ratika S Sapalya

[1]*Topiwala National Medical College, BYL Nair Charitable Hospital, Mumbai;* [2]*AIDS Research and Control Centre (ARCON), Sir. J. J. Hospital, Mumbai;* [3]*Department of Infectious Diseases, MGM Medical College, Navi Mumbai;* [4]*The University of Texas-Houston, USA*

Summary

Objective: To determine the perinatal transmission rate of HIV infection in Mumbai. **Design:** Prospective, cohort study. **Setting:** University teaching hospital with neonatal intensive care facility. **Population:** Pregnant women detected HIV-1/2 sero-positive at prenatal counselling and testing services. **Patients and Methods:** Pregnant women detected HIV-seropositive at Voluntary Counselling and Testing services were then tested for their immune status by CD4/CD8 cell counts and viral load test between 28 and 34 weeks of gestation. Protocol included prescription of Zidovudine (ZDV) from 34th week to onset of labour. Caesarean section was done for obstetric indications. New-born baby's blood was tested by RT-PCR test at birth, 2 and 6 months of age. Women were provided informed – choice for breast – feeding options. **Main Outcome Measures:** 1. Number of babies infected with HIV as determined by RT-PCR test. 2. Effect of maternal immune status and viral load on perinatal transmission rate. 3. Morbidity and mortality of HIV – infected and non-infected infants. **Results:** Between August and November 1998, of 1257 pregnant women, 50(3.9%) HIV seropositive women were recruited in the study. One opted for termination of pregnancy and 16 were lost to follow up before delivery. 4/33 women took ZDV intermittently for few days. In all, 12/33 (36.4%) babies tested at birth and/or at 6 months were RT-PCR positive. Four babies died during follow up. Perinatal transmission co-related directly with CD4 count of less than 500 cells/μL. Viral load also showed linear relationship with perinatal transmission. **Conclusions:** Higher rate of perinatal transmission among breast feeding population is documented. Cost of ZDV was unaffordable for most women attending public hospitals and hence, ZDV should be made available on cost sharing basis or free of cost. There is need for emphasis on behavioural change among young women and men through provision of voluntary counselling and testing services.
The perinatal transmission rate of HIV-1 in Mumbai among ZDV-naïve women was 36.4% and correlated directly with CD4 count of <500 cells/μL.

Introduction

Transmission of HIV infection from mother to child is a major concern for developed as well as developing countries (AIDS Watch 1998; Barbicci et al, 1991). India has just emerged with a major epidemic of HIV (Salunke et al, 1998). Sero-prevalence of HIV infection in pregnant women has increased from 0.8% in 1992 to 4.2% in 1998 in Mumbai, India (NACO, 1998). HIV- infected children are known to fall sick repeatedly and this will take away a major share of public health resources. Thus, there is an urgent need for behavioural intervention through voluntary counselling and testing services for effective control of HIV epidemic. Several studies using anti-retroviral drugs are reported to have reduced the rate of perinatal transmission (Shaffer et al 1999). Zidovudine (ZDV), a nucleoside reverse transcriptase inhibitor is said to be a potent drug known to reduce perinatal transmission without much side effects in pregnant women (Sperling et al, 1996). Mother's

immune status as derived by CD4 / CD8 lymphocyte cell counts as also by viral load correlates directly with vertical transmission rate (Mayux, et al, 1997). Intrapartum measures like vaginal douche with antiseptic lotion and policy of avoiding premature rupture of membranes also are reported to reduce the perinatal transmission (Biggar et al, 1996; Minkoff et al 1995).

Transmission of HIV infection is shown to be higher during labour in various studies done earlier (Mandelbrot et al 1996; Jeffery et al 1999). Exposure to high viral load in vaginal secretions during natural birth is reported to be the crucial event for transmission through baby's oral and nasal mucosa. (The International Perinatal HIV group, 1999). Also, gush of blood associated with shearing and separation of placenta consequent to uterine contractions before cutting of umbilical cord may be associated with high rate of transplacental transfer of the infection (Mock et al 1999).

Breast-feeding is also known to transmit HIV infection especially in early months of feeding (Miotti et al 1999). Benefits of breast feeding which are traditionally accepted in the Indian society were lost by the concept of not to breast feed the baby. Mumbai is an epicentre of HIV infection in India. In the absence of reliable data on perinatal transmission from Indian settings, we designed this study to document the events of perinatal transmission.

Patients and Methods

The study was conducted at Topiwala National Medical College and BYL Nair Charitable hospital, a teaching hospital in Mumbai. One thousand three hundred women attending antenatal clinic between August 1998 and November 1998 were exposed to information on HIV/STD, reproductive health using flip charts, video films, group talks and behavioural intervention. HIV test was offered and those who opted for the test were provided with pre-test counselling. Written informed consent was obtained in local understandable language(s) for blood test for HIV serology. Those who declined consent were provided regular antenatal care. 3-5 ml blood was collected in plain sterile test tubes and was tested by Microwell ELIZA (Biochem Immunosystems, Canada) and spot test (Organics Israel) for HIV-1/2. All women were given post-test counselling and those found to be HIV sero-positive were prescribed abbreviated Zidovudine (ZDV); 100mg five times a day, for prophylaxis from 34 weeks till the onset of labour (Shaffer et al, 1999). Immune status was assessed at 30 to 34 weeks of gestation by CD4 / CD8 count (Capsellia, Sanofi, France) and also viral load tests (Amplicor, Roche, USA). Frequent haemoglobin monitoring was planned for anaemia among women taking ZDV.

Intra-partum intervention in the form of betadine 1% vaginal douche once during labour and avoidance of premature rupture of membrane was adopted. As a policy caesarean sections were done for obstetric indications only. Baby's cord blood was collected at birth in EDTA vacutainer observing all aseptic precautions and was tested for qualitative RT PCR using primer 431/462 base-pairs (Rogers et al 1989).

HIV sero-positive women were counselled regarding breast-feeding options. Informed choice for breast-feeding was left to the couple. Babies of HIV sero-positive mothers and equal number of babies born to HIV sero-negative mothers were followed-up for one year. Baby's blood was retested by qualitative RT PCR at 2 and 6 months of infancy. Defaulting mothers were paid home visits by a counsellor to know the health status of the babies.

Data was analysed for co-factors of perinatal transmission and included immune status of mother, her viral load, role of interventions adopted and possible effects of breast-feeding using Epi-Info 5.0

Results

Of 1300 women, 1257 (96.7%) mothers consented for testing and were screened for HIV infection. 50/1257 (3.9%, CI 0.95; 2.8, 4.9) women were all found to be HIV – 1/2 sero-positive by two tests. Sixteen women were lost to follow-up before delivery. One woman opted for termination of pregnancy. The remaining 33 women delivered at the hospital (including 3 emergency caesarean sections done for various obstetric indications.) 12/33 (36.4%) babies were tested positive by qualitative RT-PCR up to 6 month's of age.

1) **Mode of delivery :** Most of our women preferred to deliver vaginally due to traditional acceptance towards natural birth. Many women were from low socio-economic class with poor personal hygiene. Wound infection and puerperal sepsis were the most feared complications amongst our women. Hence caesarean sections were done only for obstetric indications. As shown in table I, 30/33 women delivered vaginally and 11 of their babies were RT PCR positive by six months of age. Of three women who underwent caesarean delivery one had her baby HIV sero-positive at birth. None of our 6 preterm born babies were HIV sero-positive at birth or at six months of age.

2) **Role of Immune status and viral load:** CD4 count in peripheral blood showed close relationship with perinatal transmission (Table II). CD8 count did not show any definite pattern of correlation with perinatal transmission. However, the ratio of CD4 to CD8 (table III) correlated well with the perinatal transmission rate. High viral load was seen to be associated with increased rate of perinatal transmission of HIV infection (Table IV).

3) **Intrapartum perinatal transmission :** In this study vaginal douching with betadine (1%) solution once during labour was performed on 12/25 (48%) of women. 6/12 (50%) of babies born to these women were RT-PCR positive and 3/13 (23..1%) of women who did not get betadine douches were tested RT-PCR positive at birth and / or at 6 months (p=0.325). Rupture of membranes of less than 4 hours duration was associated with perinatal transmission in 8/24 (33.3%) of women. More than 4 hours of rupture of membranes was associated with transmission in 4/8 (50%) (p=0.673).

Table I : Mode of delivery & perinatal transmission

Mode of delivery	Number N=33	Babies tested positive at birth	Additional babies tested positive at 6 month	Cumulative Total (Percent)
Vaginal	30	08	03	11(36.7)
Caesarean Section	03	01	00	01(33.3)

Table II : CD4 lymphocyte counts & perinatal transmission.

CD4 Count/ml	Number N=30	Babies tested positive at birth	Additional babies tested Positive at 6 months	Cumulative total (Percent)
<200	03	02	00	02(66.6)
201 – 500	19	05	02	07 (36.8)
>501	08	00	01	01(12.5)

Table III : Correlation of CD4 : CD8 with Perinatal transmission.

Ratio CD4:CD8	Number N=30	Babies tested Positive at birth	Additional babies tested Positive at 6 months	Cumulative total (Percent)
<0.500	05	04	00	04 (80.0)
0.501 – 1.000	14	03	01	04 (28.6)
>1.001	11	00	02	02 (18.2)

Table IV: Maternal viral load and perinatal transmission.

Viral particles Per mL	Number of mothers N=30	Babies positive at birth	Additional babies tested positive at 6 months	Cumulative total (Percent)
<1000	04	00	00	00
1001-10,000	11	02	02	04 (36.3)
10,001-50,000	10	03	00	03 (30.0)
>50,001	05	02	01	03 (60.0)

Median viral load = 11,548 particles / mL

Table V : Correlation of Breast-Feeding with perinatal transmission.

Breast feed	Number of Mothers N=33	Babies tested positive at birth	Additional babies tested positive at 6 months	Cumulative total (Percent)
Yes	16	05	01	06 (37.5)
No	17	04	02	06 (35.3)

Table VI : Correlation of morbidity and mortality with HIV status of Infants.

HIV status of Infant	Number N=33	Upto 7 days	7 days to 6 months	6 – 12 months
RT-PCR positive	12	all healthy	1 died, 3 sick	3 sick
RT-PCR negative	21	2 died	1 died, 2 sick	2 sick
*Babies of HIV sero-negative mothers	50	2 died	00	00

* Data from hospital record.

4. **Role of Breast Feeding :** Breast milk has documented many advantages in a developing country like India and prohibiting or discouraging breast-feeding was found to be obviously less acceptable. There was no difference seen in perinatal transmission of HIV in breast-fed and non-breast-fed groups (Table V). Counselling for informed choice to mother whether to breast-feed or not, showed discouraging response amongst our women. However, formula milk was not supplied to babies of HIV positive women.

5. **Morbidity and mortality of Infants born to HIV sero-positive women:** The study showed that morbidity and mortality amongst RT-PCR positive and negative babies born to HIV sero-positive mothers was not significantly different (Table VI). The morbidity amongst RT-PCR positive babies was infection (septicaemia) while amongst RT-PCR negative babies, the deaths were due to birth trauma and prematurity. 6/12 (50%) of RT-PCR positive babies were sick with intercurrent infections by their first birthday.

Discussion

This study determines HIV perinatal transmission amongst ZDV-native population in India. Prescribe-and-buy policy for Anti Retroviral Therapy (ART) did not work in present study due to the high cost of therapy.

Higher rate of perinatal transmission (36.4%) was demonstrated in our women in Mumbai. Mode of delivery showed no correlation. Caesarean section performed for obstetric indications in our study did not show any increase in post-operative infection rate. Douching of vagina with antimicrobial agent during labour did not reduce the perinatal transmission, which may suggest inadequate concentration of betadine or lack of proper techniques. Prolonged rupture of membrane for more than 4 hours has shown to increase the rate of transmission, though not statistically significant. However, prolonged rupture of amniotic membranes was thought to be associated with ascending bacterial (non-specific) infection and chorio-amnionitis. Presence of chorio-amnionitis may accelerate the trans-placental transfer of HIV infection before the birth of the baby.

Rate of perinatal transmission showed linear relationship with lower maternal CD4 counts and high viral load (8). However, the CD4 count and ratio of CD4: CD8 was seen as sensitive parameters for determining the rate of transmission. In view of this, it is desirable to have facilities for CD4/CD8 estimation in early pregnancy. In order to optimise benefit of such intervention in developing countries, we need to address the following barriers: 1. Improve early attendance at prenatal clinics; 2. Establishing district-level voluntary HIV counselling and testing centres; 3. Developing simple technology for CD4/CD8 testing at district-level; 4. Making ZDV affordable for general population. This will be an additional opportunity for early intervention to reduce the burden of paediatric AIDS.

Breast-feeding decision was left to the couple to choose. Breast-feeding is traditionally accepted as the best choice. Psychological pressure of family members and financial burden of purchasing formula milk may compel women to breast-feed the child. In this study breast-feeding showed no difference in the transmission rate. Contrary to established post-natal transmission data from Africa and Thailand (Miotti et al, 1999) this study did not demonstrate any difference in horizontal transmission of HIV in breast-fed and non-breast fed babies. However, in the study the numbers were small. There could be regional variation in post-natal HIV – transmission due to several factors including the prevalence of sub-clinical mastitis. Most studies, including this have not addressed these factors. Also, level of cell free HIV-1 in breast milk seems to be determined by "Blood-breast" barrier of 41,000 virions/ml of plasma (Jaykar et al, 1999). In view of the above, we believe that the role of breast-feeding needs to be studied further.

At the end of one year 66% of perinatally infected babies were found to be healthy versus 94% of non-

infected babies. This illness correlated with poor socio-economic condition, poor maternal literacy and their understanding the concept of hygiene.

India is hit with the epidemic towards late-80's. Hence, the medical fraternity is still groping with needs of the epidemic. During the course of this study, it was observed that initial fear and apathy of doctors, technicians and nurses was replaced by gradual acceptance. This change of attitude is not-self-sustainable in a traditionally hierarchical system, and requires constant persuasion.

Acknolwedgement

Authors are thankful to the Dean, Topiwala National Medical College and BYL Nair Charitable hospital, Mumbai. The study was supported by ARCON.

References

1. AIDS watch-News from WHO South East Asia region on STD and AIDS, Vol. 3(1), Jan 1998.
2. Barbicci M, Repke JT, Chaisson RE. Lancet 337: 709, 1991.
3. Biggar RJ. Miotti PG, Taha TE, Mtinavalye L, Broadhead R, Justesen A, Yellin F, Liomba G, Miley W, Waters D, Chiphangwi JD, Goedert JJ. Lancet 347: 1647, 1996.
4. Jaykar AV, Dongaonkar DD, Hira SK, Angadi SA, Fernandes CS. LESEDI South Africa '99; STD p9: Nov' 1999.
5. Jeffery SA, Stinger MD, Swight JR. JAMA 281: 1946, 1999.
6. Mandelbrot L, Mayaux MJ, BongainA, Berrebi A, Moudoud-Jenpetit Y, lBenifla JL, Ciraru-Vigneron N, Le Chenadec J, Blanche S, Delfraissy JF. Am J Obstet Gynaecol 75:661, 1996
7. Mayaux MJ, Dussaix E, Isopet J, ReKacewicz C, Mandelbrot L, Ciraru-Vigneron N, Allarmom MC, Chanbrim V, Katlama C, Delfraissy JF, Puel J. J Infec Dis 175(1): 172, 1997.
8. Minkoff H, Burns DN, Landesman S, Youchah J, Goedert JJ, Negent RP, Muenz LR, Willoughby AD. Am J Obstet. Gynaecol 172:858, 1995.
9. Miotti PG, Taha TE, Kumvenda NI, Broadhead R, Mtimavalye LA. JAMA 282: 744, 1999.
10. Mock PA, Shaffer N, Bhadrakom C, Siriwasin W, Chotpitayasunondh T, Chearskul S, Young NL, Roongpisuthipong A, Chilnayon P, Kadish ML, Parikh B, Mastro TD. AIDS 1999; 13(3): 407, 1999.
11. National AIDS Control Organisation (NACO), Ministry of Health and Family Welfare, Government of India, New Delhi: Combating HIV/AIDS in India, 1999-2000: Current status and trends of HIV/AIDS epidemic in India. Pp-4.
12. Rogers MF, Ou CY, Rayfield M, Thomas PA, Schoenbaum EE, Abrams E, Krasinski K, Selwyn PA, Moore J, Kaul A. N Eng J Med 1989; 320: 1649, 1989.
13. Salunke SR, Shaukat M, Hira SK, Jagtap MR. AIDS 12(B): S27, 1998.
14. Shaffer N, Chnachoowang R, Mock PA, Bhadrakom C, Siriwasin W, Young NL, Chotpitayasunondh T, Chearskul S, Roongpisuthipong A, Chinayon P, Karon J, Mastro TD, Simonds RJ. Lancet 1999; 353: 773, 1999.
15. Sperling RS, Sharpiro DE, Coombs RW, Todd JA, Herman SA, McSherry GD, O'Sullivan MJ, Van Dyke RB, Jimenez E, Rouzicoux C, Flynn PM, Sullivan JL. N Eng. J Med 335: 1621, 1996.
16. The International Perinatal HIV group. N Eng J Med 340:977, 1999.