RESEARCH PAPER

Outcome of Prevention of Parent-to-Child Transmission of HIV in an Urban Population in Southern India

SUBRAMANI SEENIVASAN, NATARAJAN VAITHEESWARAN, VISWANATHAN SEETHA, *SELVARAJ ANBALAGAN, *RAMESH KARUNAIANANTHAM AND *SOUMYA SWAMINATHAN

*From Department of Pediatrics, Government Kilpauk Medical College, and *National Institute for Research in Tuberculosis (formerly Tuberculosis Research Centre); Chennai, India.*

Correspondence to: Dr S Seenivasan, 28, Indra Nagar, Walajah Road, Sholinghur, Vellore, Tamilnadu 631 102, India. seeni.sholing@gmail.com

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Objective: To analyze the outcomes of Prevention of Parent to Child Transmission (PPTCT) of HIV program in an urban Southern Indian setting.

Design: Observational study.

Setting: Anti-retroviral Therapy (ART) Centers/ Integrated Counseling and Testing Centers (ICTC) at four government Obstetrics Institutes in an urban area.

Participants: 100 HIV-positive pregnant women and their infants delivered in the study centers.

Methods: Triple drug ART to HIV-positive pregnant women was started for maternal indications only. Rest of the pregnant women were given single dose Nevirapine (200 mg) at the onset of labor. All infants were given single dose Nevirapine (2 mg/kg) prophylaxis, according to National AIDS Control Organization guidelines. Mothers were counseled regarding breastfeeding and artificial feeding, and the choice was left to them. Whole blood HIV 1 DNA PCR was done for all infants at 6 weeks of life. A second PCR was done at 6 months or 6 weeks after stopping breastfeeds. PCR-positive infants were started on ART, and were followed-up till18 months of life.

Results: Four infants were PCR-positive for HIV. All of them were breastfed. They were born to mothers of HIV stage 1 or 2 who were not on ART as CD4 counts were >350 cells/mm^3. Among the mothers in Stage 3 or 4 or CD4 count <200 cells/mm^3 and on ART, none of the infants was HIV-positive. The cumulative HIV-free survival at 18 months was 94%.

Conclusion: Parent-to-child transmission rate in HIV was low with the currently used strategies . Triple drug ART to mother reduces mother-to-child transmission despite advanced maternal stage or low CD4 counts.

Keywords: *HIV-1 DNA PCR, HIV programme, PPTCT.*

Though children represent only 6% of the HIV-infected population, they contribute to one-sixth of HIV-deaths [1]. More than 95% of HIV infections in children are due to vertical transmission [2]. Deaths due to HIV in children can be reduced through effective implementation of Prevention of Parent-to-Child Transmission (PPTCT) program, and by using antiretroviral therapy in HIV-infected children. When this study was started, National AIDS Control Organization (NACO) recommended single dose Nevirapine prophylaxis to both mother and baby with an anticipated reduction of mother-to-child transmission rate to 10-20% [1].

This study was undertaken to analyze the outcomes of PPTCT services in an urban population in Southern India, and to study the factors influencing vertical transmission of HIV.

METHODS

The study was undertaken in the Antiretroviral Therapy (ART) center and Integrated Counseling and Testing Center (ICTC) at four government Obstetric Institutes in Chennai, India from January 2009 to Febuary 2012 (including 18 months follow up). All pregnant women in the study setting from January 2009 to August 2010 were screened for HIV by ELISA test. HIV-positive pregnant women referred from distant places for institutional delivery, and those who were unlikely to be followed for 18 months for any reasons, were excluded. The study was conducted after the Institute's ethical approval and informed written consent of the parents.

Accompanying Editorial: Pages 750-52.

Those tested positive for HIV were classified into four clinical stages according to the WHO guidelines [3]. CD4 counts were done in all HIV-positive women. Triple drug ART (Zidovudine, Lamivudine and Nevirapine) was started in pregnant women who were in WHO clinical stage 4, stage 3 with CD4 <350 cells/mm^3, and those with stage 1 and stage 2 with a CD4 count of <200 cells/mm^3.

Single dose (200 mg) Nevirapine was given to all the other HIV-positive pregnant women at the onset of labor and to the neonates (2 mg/kg) soon after delivery [1]. All women were counseled regarding breastfeeding and replacement feeding (undiluted cow milk or formula feed), and the choice was left to them. If a woman chose to breastfeed, exclusive breastfeeding was advised up to 6 months and to switch over to replacement feeds. Thereafter mixed feeding was not advised. Replacement feeding in the first 6 months was given only if it was Acceptable, Feasible, Affordable, Sustainable and Safe (AFASS) [1,4]. A child was defined as 'breastfed' if he/she was breastfed for anytime from birth to six months. A child was defined as non-breastfed if he/she was not at all breastfed after delivery. No child from both the groups was breastfed after six months. Infants of all HIV-positive mothers were followed up for 18 months.

Three mL of blood was collected in vacutainer containing EDTA. DNA PCR testing was performed using Amplicor HIV-1 DNA v1.5 kit (Roche molecular Diagnostics, NJ, USA). CD4/CD8 T cell counting was performed on the BD FACSCalibur flow cytometer. CD4/CD8 percentage and absolute counting was performed according to the instructions provided by the manufacturer. Whole blood HIV 1 DNA PCR was done for all infants at 6 weeks of age. If the infant was PCR-positive, the test was repeated with a new blood sample as soon as possible, to confirm diagnosis before disclosure to parents. A second PCR test was done in all PCR-negative infants at 6 months or 6 weeks after stopping breastfeeds [1]. A negative test was disclosed only after the second PCR test was negative, and the child was no longer exposed to breastfeeds. All children were followed up to 18 months with assessment of nutritional status and for evidence of any clinical markers of HIV like oral candidiasis, recurrent respiratory infections, chronic suppurative otitis media, lymphadenopathy, hepatomegaly, parotid swelling, eczema, and molluscum contagiosum, at each visit. HIV ELISA was done at 18 months of age. ART was started to HIV-positive babies according to NACO guidelines [1]. ART regimen was triple drug (Stavudine, Lamivudine, Nevirapine) as Fixed Dose Combination (FDC) based on weight of infant.

RESULTS

There were 79,268 deliveries during the study period; 176 (0.22%) mothers were HIV ELISA positive (***Fig.*1**). Seventy-six mothers were excluded because they were referred from distant secondary-care hospitals for delivery or because they were unlikely to be followed for 18 months for social reasons.

One hundred included women were divided into three groups based on CD4 counts <200 (*n*=5), 200 to 350 (*n*=19) and >350 (*n*=76). HIV clinical staging in pregnant women was Stage 1 (*n*=33), Stage 2 (*n*= 55), Stage 3 (*n*=10) and Stage 4 (*n*= 2). Thirty seven mothers were on

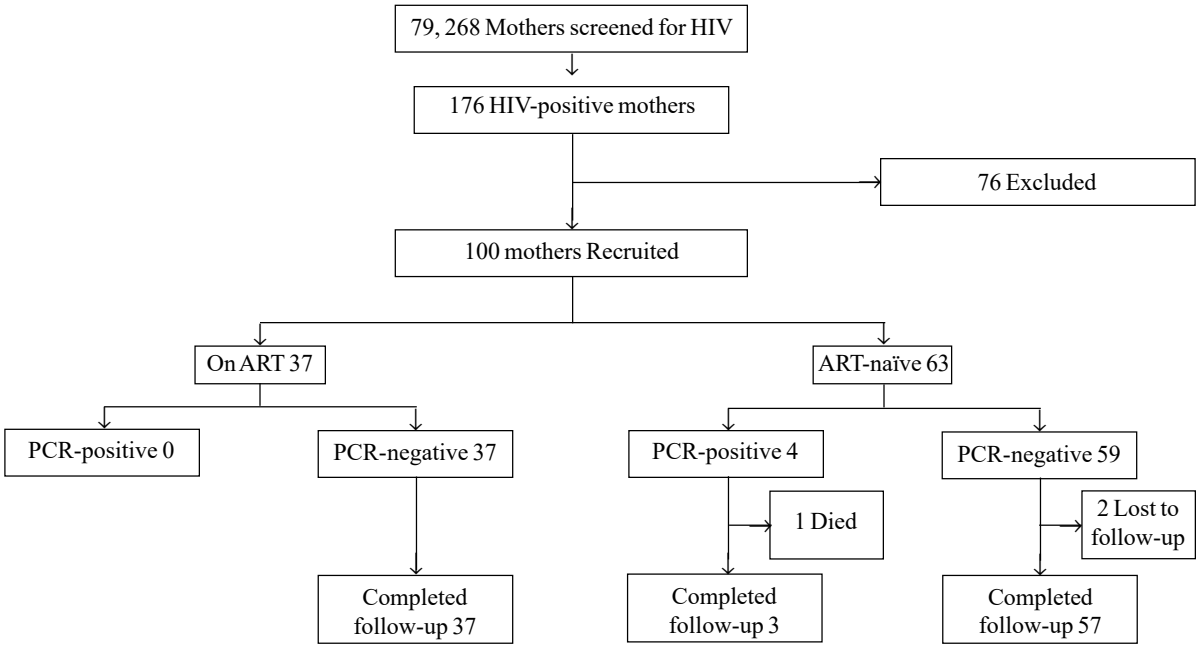

FIG.1 *Study population and follow-up.*

triple drug ART. The median gestational age of starting ART was 16 (IQR 0, 28) weeks. The mean (SD) birth weight of the infants was 2710 (344) g. Twelve were born preterm. Forty-two infants were born by vaginal delivery and 58 by Caesarean section.

All 100 neonates received single dose Nevirapine soon after delivery. Sixty mothers chose to breastfeed. Among the breastfed, only three infants were breastfed for the entire 6 months; others were breastfed for variable periods from 1 month to 5 months and were switched to replacement feeds. The median (IQR) duration of breast feeding was 3 (2, 3.5) months. Forty mothers chose replacement feeds (artificial formula or undiluted cow's milk) from day 1 of life. There was no mixed feeding.

Three infants were HIV DNA PCR-positive at 6 weeks and 97 were negative. Among babies tested negative, the second sample at 6 months yielded one more positive result. The details of PCR-positive infants are given in ***Table* I**. Two infants were born to mother with stage 1 disease and other two with stage 2 disease. No child born to mothers with stage 3 or 4 who were on ART developed HIV positivity. CD4 counts of mothers of four positive infants were more than 350/mm^3. All the four positive infants were referred to Pediatric ART Center at Institute of Child Health. One child died of broncho-pneumonia at 6 month of age; his CD4 count was 1880 cells/mm^3 (27%). Two of the PCR-negative babies were lost to follow up.

TABLE I MATERNAL HISTORY AND PROFILE OF HIV-1 DNA PCR-POSITIVE INFANTS

	A	*B*	*C*	*D*
Maternal history				
Age (y)	23	31	30	27
Weight (Kg)	45	66	57	56
Gravida	Primi	Primi	$G_4P_3L_3A_0$	$G_2P_1L_1A_0$
CD4 Count (Cell/mm^3)	467	834	890	491
HIV Stage	1	1	2	2
ART status	No	No	No	No
Spouse HIV status	Positive	Positive	Positive	Positive
Bleeding PV	Yes	No	No	Yes
PROM >4 hours	No	No	No	No
Infant demographics				
Gender	Male	Female	Male	Female
Birth Weight (g)	2500	2900	2250	3000
Mode of delivery	LSCS	LSCS	Vaginal	Vaginal
Nevirapine	Yes	Yes	Yes	Yes
*Duration of breastfeeding	3 mo	4 mo	2 mo	4 mo
HIV stage	Stage 1	Stage 1	Stage 1	Stage 1
CD4 Count (cells/mm^3)	3411	2718	1880	1898
CD4 %	47 %	41 %	27 %	32 %
CD8 Count (cells/mm^3)	1161	1859	2437	2140
CD8 %	16	26	35	36
CD4 / CD8 Ratio	2.94	1.46	0.77	0.89

ART- Anti Retroviral Therapy, LSCS- Lower Segmental Caesarean Section, PROM- Prolonged Rupture of Membrane.
**All infants were breastfed exclusively.*

DISCUSSION

The overall parent-to-child transmission rate in this study was 4%; it was 6.3% with single dose Nevirapine alone. This transmission rate was less than the expected 10 to 20% in a pilot study done by NACO [1]. However, it was similar to a study from Chennai with an overall transmission rate of 8.3% from a sample of 218 dried blood spot DNA PCR [5]. Others have shown even higher transmission rates [6,7]. Marinda, *et al*. [8] showed HIV-positive mothers with more advanced disease are more likely to infect their infants. However, in our study, all 4 PCR-positive babies were born to mothers who were in stage 1 or stage 2, and whose CD4 count was >350 cells/mm^3. Marazzi, *et al*. [9] showed a transmission rate of 50.6% from mothers with CD4 count >350 cells/mm^3 but these women were not on ART. Ugochukwu, *et al*. [10] found lower transmission rates when both mother and baby were on prophylaxis. This shows that triple drug ART reduces the transmission rate even in advanced maternal disease or in the presence of low CD4 counts. Moreover, recent guidelines and several studies recommend triple drug regimens to prevent parent-to-child transmission of HIV [11-13]. Single dose Nevirapine may also be associated with increased risk of resistance [14].

Though transmission rates were 6.7% and 0% in breastfed and non-breastfed groups, respectively; we do not attribute PCR positivity to breastfeeding alone as three of the four infants were PCR-positive at 6 weeks of life. This was probably due to intrapartum transmission. Palombi, *et al*. [15] showed a transmission rate of <2% with alternatives to breastfeeding without an increase in mortality in non-breastfed group. The cumulative HIV-free survival at 18 months in our study was similar to that reported in an earlier study [9].

The limitations of our study were small sample size, and that our study population mostly belonged to lower and lower-middle class which may not be representative of the entire population.

We conclude that the overall parent-to-child transmission rate of HIV is low when the pregnant women receive ART, and single dose Nevirapine is given to the infants, simultaneously avoiding mixed feeding.

WHAT IS ALREADY KNOWN?

- Parent-to-child transmission of HIV occurs with advanced maternal disease and low CD4 counts.

WHAT THIS STUDY ADDS?

- Most of vertical HIV transmissions occur when mothers are not on triple drug ART.
- Parent-to-child transmission rate with single dose Nevirapine prophylaxis to mother and baby is low.

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