

Effect of ART Prophylaxis and Infant Feeding Practices on Transmission of HIV from Parent to Child during First 6 Months of Life.

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Abstract:

Background: Globally, the number of children younger than 15 years living with HIV infection had increased from 1.6 million in 2001 to 2.5 million in 2009. In 2009 globally, 370,000 children under the age of 15 years were newly infected, i.e. approximately 1000 a day and 260,000 children died, the majority were under the age of 2 years. As the perinatal transmission is major route of transmission of pediatric HIV, much work is to be done in this area to improve the care of the HIV positive mothers i.e. regarding ART prophylaxis, institutional deliveries, proper infant feeding practices and follow up care.

Objectives: To study risk of transmission of HIV from mother to child during pregnancy and breast feeding and to study the role of infant feeding practices in breast feeding related HIV transmission.

Methodology: Prospective observational study was done at PCOE-Pediatric centre of excellence, Niloufer hospital for women and children. Included 58 HIV positive (infected) mothers, who were registered at PCOE-Niloufer hospital from August 2014 to October 2015. The babies, were tested by DBS-Dried Blood Spot test method at 6 weeks and 6 months to detect infected babies.

Results: Mean age of the mother is 24.63 years. Mean birth weight is 2.63kg. 79% babies were on exclusive breast feeding, 17% babies were on formula feeds and 4% babies were on mixed feeding. PCR done at 6 (45 DAYS) weeks of age out of 58 babies 57 babies were tested found to be non reactive one baby died at the age of one month before doing the test. For 41 eligible babies PCR done at 6 (180 DAYS) months of age revealed 93.7% nonreactive and 7.3% reactive for HIV. There was significant relationship found between PCR 180 and type of feeding. 100% transmission was found in mixed feeding babies, 3.2% in breast feeding babies and none of them were positive in exclusive replacement feeding babies.

Conclusion: Adherence to ART during pregnancy (TDF + 3TC + EFV), prophylactic Nevirapine during first 6 weeks of birth and exclusive breast feeding are the mainstay of reducing perinatal transmission of HIV in children.

Keywords: ART prophylaxis, infant feeding practices, PPTCT.

I. Introduction

Children represent only 6% of all people infected with HIV/AIDS. They account for 18% of the 3.1 million AIDS deaths. Only 4 percent of the one million people who are now on antiretroviral treatment are children. India has an estimate 202,000 children infected by HIV/AIDS (UNAIDS 2004). Approximately 56,700 HIV infected infants, is added every year (NACO, 2005). About 45,000 individuals on ART through public, private, and NGO supported ART centers (NACO 2006). There are 2,300 children, who are currently receiving ART in India (NACO Oct, 06). However, half of HIV-positive children die undiagnosed before their second birthday. The reasons include lack of access for treatment of children with HIV/ Issues of diagnosis in infants (early diagnosis), lack of clear guidelines for the treatment of children, lack of access to appropriate pediatric ART formulations, inadequate capacity and knowledge of service providers in clinical management of Pediatric, Lack of surveillance and data in this age group. As the perinatal transmission is major route of transmission of pediatric HIV, much work is to be done in this area to improve the care of the HIV positive mothers i.e. regarding ART prophylaxis, institutional deliveries, proper infant feeding practices and follow up care. The work was done to know the risk of HIV transmission during pregnancy and breast feeding and to know the infant feeding practices in the resource poor settings.

II. Aims And Objectives

1. To study risk of transmission of HIV from mother to child during pregnancy and breast feeding.
2. To evaluate the relationship between various maternal factors, CD4 count/type of delivery and risk of HIV transmission

3. To study the role of infant feeding practices in breast feeding related HIV transmission

III. Methodology

Study design: Prospective observational study.

Approval: This study received approval from college ethical committee.

Setting: At PCOE-Pediatric centre of excellence, Niloufer hospital for women and children, Hyderabad.

Study group: 58 HIV positive (infected) mothers, who were registered at PCOE-Niloufer hospital.

Study period: 15 months, from August 2014 to October 2015

Inclusion criteria:

1. Mothers who are HIV positive, registered at PCOE and willing to participate in the study.
2. Those HIV positive mothers who were given antenatal ART prophylaxis.
3. The babies of HIV positive mothers who were given Nevirapine prophylaxis for 6 weeks.

Exclusion criteria:

1. Mothers who are HIV positive registered at PCOE, not willing to participate in the study.
2. Those HIV positive mothers who were not registered at PCOE –Niloufer hospital.
3. Those HIV positive mothers who were not on antenatal ART prophylaxis.
4. The babies of HIV positive mothers who were not given Nevirapine prophylaxis for 6 weeks.

Methodology

The study was commenced after taking approval from the ethics committee of Osmania Medical College. After obtaining written consent mothers were interviewed and followed up at PCOE-Niloufer hospital. A semi structured questionnaire was given to these mothers which included identification data, antenatal history, parity, CD4 count prior to the delivery, place of the delivery, type of the delivery (normal vaginal delivery or lower segment caesarian section), APGAR score, Term/Pre term baby, weight, type of feeding (Exclusive Breast feeding (EBF) or Top feeding (Exclusive Replacement Feeding) or mixed feeding) were recorded on case proforma. Mothers were started on TLE regimen and babies were given nevirapine prophylaxis for 6 weeks as per NACO guidelines and were closely followed up.

The babies were tested (DBS-Dried Blood Spot test) by heel prick method at 6week and 6months to detect infected babies .The total number of babies eligible for the test at 6weeks are 57 as one baby died at 1month of age among 58 included babies and total number of babies eligible for the test at 6months are 41babies. The test was done by DNA PCR method collected samples were sent to MGR University, Guindy located in Chennai for analysis through proper channel as directed by NACO.

FIG 1: DBS-Dried Blood Spot test



Data Analysis

A master chart was prepared with all the data that was collected. MS excel sheet was used to summarize the data and SPSS version 19 software was used for analysis of data. Chi squared test is used to know the relationship between various factors. The results are then compared with other studies.

IV. Observations And Results

Total numbers of mothers in the study (n) were 58. Majority of mothers were in the age group of <25 years (48%), 47% belongs to 25-30 years and 5 % are >30 years of age. Mean age of the mother is 24.63 years. 50% belongs to G2, 35% are primi, 12% are G3, and 3% are G4. Out of 58 mothers 64 % (37) had CD4 count of >350, 26 % (21) had CD4 count <350. 69% babies born through normal vaginal delivery, 22% delivered by elective caesarian section and 9% delivered by emergency caesarian section. 52% are male babies and 48% are female babies. 22% had low birth weight, 78% had normal birth weight. Mean birth weight is 2.63kg. 79% babies were on exclusive breast feeding 17% babies were on formula feeds and 4% babies were on mixed feeding. PCR done at 6(45 DAYS) weeks of age out of 58 babies 57 babies were tested found to be non reactive one baby died at the age of one month before doing the test. For 41 eligible babies PCR done at 6(180 DAYS) months of age revealed 93% nonreactive and 7% reactive for HIV.

TABLE 1: Relationship between Risk of Transmission through Breast Feeding (Pcr180), Age Of mother, Birth Weight and C4 Count.

T-Test, Group Statistics

	Pcr_180		Mean	Std. Deviation	Std. Error Mean
Age of mother	Non Reactive	38	24.34	3.604	.585
	Reactive	3	26.00	.000	.000
Birth weight	Non Reactive	38	2.634	.4966	.0806
	Reactive	3	2.533	.0577	.0333
CD4Count	Non Reactive	38	413.58	271.946	44.115
	Reactive	3	822.00	661.371	381.84

There is no significant relation between REACTIVE test atPCR180 with Age of mother, birth weight and CD4 count

TABLE2: Risk of Transmission through Type of Delivery

Type of delivery	PCR 180		
	Non Reactive	Reactive	Total
Elective caesarian section	10(90.9%)	1(9.1%)	11
Emergency caesarian section	3(100%)	0	3
Normal vaginal delivery	25(92.6%)	2(7.4%)	27
total	38(92.7%)	3(7.3%)	41

Chi-Square Tests

	Value	Df	Asymp. Sig. (2-sided)
Pearson ChiSquare	.288a	2	.866
Likelihood Ratio	.504	2	.777
N of Valid Cases	41		

There is no significant relationship between PCR180 and type of delivery (p value>0.05)

TABLE3: Relationship between Risk of Transmission through Breast Feeding (Pcr180) and Type of Feeding

Type of feeding	PCR 180		
	Non reactive	Reactive	Total
Exclusive breast feeding	30(96.8%)	1(3.2%)	31
Exclusive replacement feeding	8(100%)	0	8
Mixed feeding	0	2(100%)	2
Total	38(92.7%)	3(7.3%)	41

Chi-Square Tests

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	26.730a	2	.000
Likelihood Ratio	12.629	2	.002
N of Valid Cases	41		

There is significant relationship between PCR180 and type of feeding .100% transmission was found in mixed feeding babies,3.2% in breast feeding babies and none of them were positive in exclusive replacement feeding babies . Relationship between PCR 45 and other parameters i.e. age, parity, cd4count, type of delivery, weight of the baby, term/preterm is not possible as all the babies tested at 45days are non reactive (negative).

V. Discussion

HIV positive mothers were started on ART prophylaxis with TLE regimen as soon as their pregnancy was confirmed as per the NACO guidelines. They were followed up and the risk of transmission was assessed. Initiations of ART in pregnant women were done at the earliest and were counseled for adherence to maintain her own health and also to prevent HIV virus transmission to the unborn baby. According to NACO PPTCT (Prevention of Parent To Child Transmission) guidelines, in HIV infected pregnant women the dictum should be “do not delay ART initiation”. Initiate lifelong ART in all pregnant women with confirmed HIV infection regardless of WHO clinical stage or CD4 cell count. TDF + 3TC + EFV regimen (Tenofovir (TDF) (300 mgs) + Lamuvidine (3TC) (300 mg) + Efavirenz (EFV) (600 mg) at any gestational age is recommended as first-line ART in pregnant and breastfeeding women (1, 2). Infants who are either on exclusively breastfeeding or on

exclusive replacement feeding should receive ARV prophylaxis with daily Nevirapine for at least 6 weeks^{1,2}. Infant prophylaxis should begin at birth or when HIV exposure is known. As per WHO's estimate in South-East Asia Region, India has the highest burden of new paediatric HIV infections. Recommended ART could reduce the risk of MTCT to less than 5% (or even lower) in breastfeeding populations from a background risk of 35% and to less than 2% in non-breastfeeding populations from a background risk of 25%, and improve maternal and child survival. With These new interventions paediatric HIV eliminated in High-burden and resource-limited countries, which has already been achieved in many developed countries³.

Nathan Forda et al did not find any evidence of an increased risk of congenital anomalies in general, or increased risk of neural tube defects, associated with efavirenz exposure during the first trimester of pregnancy and provides the supporting evidence for WHO's 2013 recommendation that efavirenz should be part of the recommended first-line ART regimen⁴. Guidelines from the British HIV Association recommend using efavirenz in pregnancy⁵. The European AIDS Clinical Society⁶ recommends avoiding efavirenz during the first 8 weeks of pregnancy. A recent report from France suggested an increased risk of neurologic defects among infants born to women receiving efavirenz during the first trimester of pregnancy⁷. Ekouevi DK et al also supports use of efavirenz based regimen⁸. This study support use of efavirenz in pregnant women as neither pregnant women nor infants had adverse reactions and no birth defects were noted. Nevirapine has been shown to be well tolerated in both adult and pediatric patients. In a study done by Laura A et al, intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 concluded Nevirapine lowered the risk of HIV-1 transmission during the first 14–16 weeks of life by nearly 50% in a breastfeeding population⁹. In our study Nevirapine was given for 6 weeks postnatally reduced transmission rate by 92.7% during first 6 months of age.

HIV is transmitted by breast milk as proved by many studies. Firstly both the free and cell bound HIV has been isolated from human breast milk. Free HIV can infect CD4 cells lining the gastrointestinal tract of the baby. Infected maternal mononuclear cells present in breast milk can pass through mucous membranes of baby & infect the baby. Transmission to child is shown to occur from the mother infected with HIV post nately and who breast fed the infant. Studies done have compared rate of vertical transmission in those babies who were breastfed compared to those who were exclusively top fed and showed that there is 5-20% extra risk related to breast feeding depending on the length of the breast feeding. HIV has been shown in high titers in colostrums. Conditions like breast abscess, mastitis or sore nipple can lead to contamination of breast milk with mother's blood. In the present study one subject who was tested positive did not complain the above conditions. Presence of lipoproteins and other substances like mucins, lysozymes, lactoferrins, T cells, complements and secretory leucocyte protease inhibitor (SLIP) decrease binding of pathogenic organisms to GI Tract epithelial cells and decreasing chances of transmission via breast milk. Presence of anti HIV antibodies especially anti gp120, anti gp 40, IgG as well as anticore IgM & IgA antibodies in human milk have been shown by western blot technique also decrease the chances of HIV transmission to baby. recommendation for infants of HIV-infected mothers range from formula feeds with no breastfeeding at all (the ideal) to short periods of exclusive breastfeeding, followed by replacement feeding depending on the acceptability, feasibility, affordability, sustainability, and safety of the latter^{10,11,12}. As per NACO guidelines Nutritional care of children living with HIV is a fundamental part of the continuum of care and support under the national programme. Practice exclusive breast feeding for the first 6 months and avoid mixed feeding¹³. World health organization currently recommends exclusive breast feeding is the ideal method for infants during first 6 months¹⁴. A baby on top feeding has leaky gut allowing increased chances of HIV absorption. Hence, a child who is on mixed feeding will have worst outcome. Besides, such a child is exposed to evils of both HIV as well as other infections.

There is cumulative increase in transmission of HIV proportional to the length for which breast feeding continues, as shown in the Miotti et al study¹⁵. The risk was estimated to be 0.7% per month for 0-6 months (cumulative risk of 4.2% for 0-6 months), 0.6% per month between 6-12 months (cumulative risk of 3.6% for 6-12 months), 0.3% per month between 12-18 months (cumulative risk of 1.8% for 12-18 months) and 0.2% per month between 18-26 months (cumulative risk of 1.2% for 18-24 months). The total cumulative risk was estimated to be 10.2% if breast feeding was continued till 2 years. Keith Alcorn in his study concluded that postnatal transmission at months 6, 12 and 18 was 3.9%, 7.7% and 12.1% respectively. Sixty-eight per cent of infections due to breastfeeding occurred after month 6, with the highest rate of transmission in the mixed feeding group¹⁶. In Coovadia HM et al shown that HIV transmission rate was high in mixed feeding group compare to exclusive breast feeding group (hazard ratio 10.9). Cumulative 3-month mortality in exclusively breastfed infants was 6.1% (4.74-7.92) versus 15.1% (7.63-28.73) in infants given replacement feeds (HR 2.06, 1.00-4.27, p=0.051)¹⁷. In our study 100 % babies were reactive in mixed feeding group, only 3.2% were reactive in breast feeding group during first 6 months of age. Study done in Durban, South Africa compared HIV transmission in exclusive breast fed, exclusively top fed and mixed fed babies. Long term follow up results at 15 months showed that HIV transmission was 24.7% in breast fed, 19.4% in top fed and 35% in mixed fed babies¹⁸.

According to DE COOKKM et al estimated risk of HIV infection from Mother to child transmission (MTCT) in the absence of interventions during pregnancy is 5–10%, during labor and delivery is 10–15%, during breast feeding is 5–20%. Overall risk without breast feeding is 15–25%, overall risk with breast feeding 0 to 6 months is 20–35% and Overall risk with breast feeding 18 to 24 months is 30–45%¹⁹. According to Elaine et al risk can be reduced to less than 2% if mothers were kept on antenatal prophylaxis²⁰. The risk of transmission of HIV when the mother is on antenatal prophylaxis is very less. In the present study the risk is zero percent. The strength of the present study is the identification of the eligible mothers and meticulous care at every step of the study and follow up for timely laboratory diagnosis and they were advised accordingly.

VI. Conclusion

The risk of transmission of HIV is less when both the mother and child with prophylactic ART during pregnancy and breast feeding. The risk of transmission of HIV during pregnancy is zero in the present study when mother is on prophylactic ART irrespective of CD4 count and type of delivery. Cumulative risk of transmission through breast feeding, top and mixed feeding is 7.3%. The risk of transmission through Exclusive Breast Feeding is 3.2%. Risk of transmission through mixed feeding is 100%. The risk of transmission of HIV and the risk of death is more with mixed feeding. Adherence to ART during pregnancy (TDF + 3TC + EFV), prophylactic Nevirapine during first 6 weeks of birth and exclusive breast feeding are the mainstay of reducing perinatal transmission of HIV in children.

VII. Limitations

1. The sample size is small to extrapolate it to the general population.
2. Viral load was to be done who were tested REACTIVE at 6 months to correlate with the risk of transmission.
3. Maternal nutritional status i.e. MUAC (mid upper arm circumference) and hemoglobin estimation was to be done to correlate it with risk of transmission.
4. Follow up was to be done in the present study to know the risk of transmission at 12 months and to know the infant feeding practices.

VIII. Recommendations

1. The present study reinforces the recommendation of WHO the risk of transmission of HIV through pregnancy and breast feeding is less with ART prophylaxis.
2. The present study recommends giving Exclusive Breast Feeding or Exclusive Replacement Feeding but not mixed feeding.
3. The present study emphasizes the importance of Exclusive Breast Feeding.
4. Follow up studies and large hospital and field studies are needed to establish the facts and reinforce the recommendations.
5. Myths and misconceptions regarding breast feeding should be addressed sensitively and using various modes of communication to continue exclusive breast feeding.
6. Training of health workers and volunteers should focus on counseling and correct method of breast feeding in order to effectively address the breastfeeding problems to continue exclusive breast feeding.

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