ORIGINAL ARTICLE

EVALUATION OF THE INCIDENCE OF VERTICAL TRANSMISSION OF HIV INFECTION FROM SEROPOSITIVE MOTHER TO BABY WITH ART (INTERVENTION WITH NEVIRAPINE)

L. Jhansi Rani¹, G. Vanaja², Helena Bandi³, Divya Shravani Kaminedi⁴

HOW TO CITE THIS ARTICLE:

L. Jhansi Rani, G. Vanaja, Helena Bandi, Divya Shravani Kaminedi. "Evaluation of the Incidence of Vertical Transmission of HIV Infection from Seropositive Mother to Baby with Art (Intervention with Nevirapine)". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 46, June 08; Page: 8018-8027, DOI: 10.14260/jemds/2015/1165

ABSTRACT: HIV is a major global health problem. **AIM:** of the study is to identify the antenatal women who are HIV Positive and evaluate the incidence of vertical transmission from mother to baby with ART. **STUDY DESIGN:** It is a prospective cohort study. All the pregnant women who attended the antenatal OPD in Government Victoria Hospital, Andhra Medical College, Visakhapatnam between October 2013 to March 2015 were evaluated. **MATERIALS AND METHODS:** HIV screening was done using rapid stick test to all the pregnant women who attended the OPD. 7100 members were screened. 65 subjects were HIV Positive and confirmed by using Elisa Technique. They were given Anti-Retroviral Therapy. During labour 200mg tablet of Nevirapine is given to parturient and the new born babies were given Nevirapine syrup. **RESULTS:** Of the 7100 members screened, 65 (0.91%) were HIV positive. Of them 54 members came for follow up and delivered at Government Victoria Hospital. Of the 54 new born babies, 2 babies did not come for follow up. Out of 52 babies, 51 are negative and 1 baby is HIV positive after 6 weeks. **CONCLUSION:** The present study shows that incidence of vertical transmission from HIV Positive mother to baby with ART intervention is 1.96% and the efficacy of Nevirapine is 98.04%.

KEYWORDS: Highly active anti retro viral therapy (HAART), Human immunodeficiency virus, immune system, retrovirus, nevirapine, Nucleoside reverse transcriptase inhibitor(NRTI), Non-nucleoside reverse transcriptase(NNRTI), post-test counseling, pretest counseling, vertical transmission.

INTRODUCTION: The rising prevalence of HIV among pregnant woman in INDIA is of great concern. Human immunodeficiency virus is a retrovirus that attacks the immune system and if untreated, can have potentially serious consequences. Mother to child transmission has been an area of extensive research for the past two decades. In 1993, with virtually no interventions the rate of transmission was 25.6%.⁽¹⁾ Treatment with effective highly active anti retro viral therapy(HAART) not only leads to a long and healthy life in the general population, but also greatly reduces the chance of mother to child transmission. Routine antenatal screening of HIV combined with advances in HAART has led to increased detection and effective treatment in pregnancy.

National AIDS control programme phase-3 (NACP-3) has got a long term objective of testing of 22 million people inclusive of all antenatal women.⁽²⁾ Later is being done with purpose of linking seropositive antenatal women with ART as soon as possible in order to derive maximum benefit to prevent opportunistic infections and to provide single dose nevirapine to both mother and child to prevent vertical transmission.

UK data presented in 2010 showed that for pregnant women with a base line viral load >10,000 HIV RNA copies/ml, the probability of achieving an undetectable level at 36 wks. (The time

ORIGINAL ARTICLE

at which delivery management decisions must be made) is compromised by delaying initiation of HAART beyond 20.4 weeks (Cohort data in UK and IRELAND between 2000-2006 estimated the mean starting gestational age at 25.6 weeks). This data also showed that virological control to <50 HIV RNA copies /ml was achieved in only 37% of women at the time of delivery.^(3,4)

The base line HIV-1 viral load is substantial risk factor for MTCT in HIV pregnancies and then the timing and choice of treatment must be adjusted accordingly. With an aim to reduce the viral load to <50 HIV RNA copies/ml, HAART should be considered early in pregnancy, usually avoiding the first trimester. The recommended regimen based on two NRTI (Nucleoside reverse transcriptase inhibitor) plus one NNRTI (Non-nucleoside reverse transcriptase inhibitor) or boosted Protease inhibitor.⁽⁵⁾

There is a widening gulf between the effectiveness of intervention for preventing mother to child transmission of HIV. Infection to new born is transmitted by mother antenatally and perinatally, however considering the role of male partner in the transmission of infection to a woman, in India it is termed as parent to child transmission. In the absence of intervention, the vertical transmission rate is estimated to be 30% to 33% which drops down to 3% to 5% with effective antenatal, intranatal and postnatal prevention of parent to child transmission of HIV. Intrapartum Nevirapine antiretroviral prophylaxis and viral load based ART to antenatal mother, mode of delivery, and infant feeding are considered to be the major determinants for seropositivity in children born to these women.⁽⁶⁾

AIMS AND OBJECTIVES:

1. To know the incidence of vertical transmission of HIV seropositive mother to baby with intervention with anti-retroviral therapy.
2. To screen all the antenatal women attending the antenatal outpatient department in Government Victoria Hospital, Visakhapatnam from October 2013 to March 2015.
3. To know the perinatal outcome of babies born to HIV seropositive women.

MATERIALS AND METHODS: Pregnant women registering at Government Victoria Hospital, Visakhapatnam from October 2013 to March 2015 are given pretest counseling at ICTC in groups with an average of three women for 20 to 40 minutes. With obtained written consent they are tested for HIV by three compulsory rapid tests and results whether positive or negative are shared by the ICTC counselor along with individual posttest counseling. The order of these tests is prefixed by National Aids Control Organization (NACO) and subsequently by respective State Aids Control Society (APSACS for Andhra Pradesh).

Seronegative pregnant women are counseled on HIV prevention and risk reduction behavior. HIV seropositive pregnant women are additionally provided psycho social support on disclosure issues and spouse testing, linkage to ART services, importance of institutional delivery and intrapartum sdNVP, post-partum follow-up and infant feeding.

During the delivery of seropositive pregnant woman, a single dose regime of nevirapine 200 mg tablet is given at the time of onset of labour and nevirapine syrup 2mg/kg of body weight is offered to the babies within 72 hrs of birth.⁽⁷⁾ Nevirapine syrup 0.2ml/kg once daily given for 6weeks (Extended up to 12 weeks).

Exposed children are tested at birth, 6 weeks, 6 months and 12 months or 6 weeks after stopping breast feeding and confirmation with antibody test at 18 months by HIV DNA-PCR testing.⁽⁸⁾

Inclusion Criteria:

1. Female $\geq$ 18 yrs. of age.
2. Pregnancy confirmed by urine pregnancy test or ultrasonography.
3. The woman has been instructed and is willing to provide written informed consent to participate in this programme.

Exclusion Criteria:

1. Antenatal women with other coexisting HBsAG positive, HCV infections.

RESULTS AND ANALYSIS: Of all 7100 antenatal women screened, 65 were HIV positive (0.91%). The prevalence rate in our institute is 0.91%. Of them only 54 antenatal women turned for follow up and delivered in our institute.

Age distribution:

- 70% subjects were aged between 18 to 20 yrs.
- 26% were between 21 to 25 yrs.
- 4% were between 25 to 30 yrs.

Parity:

- 70% were primigravidas.
- 26% were second gravidas.
- 4% were third gravidas.

Gestational age at the time of delivery:

- 94% were delivered at term.
- 6% delivered preterm.

Mode of delivery: 85% delivered by normal vaginal delivery 13% delivered by Caesarean section 2% delivered by instrumental delivery.

Birth weight of Babies: 6% were less than 2 kgs, 37% were 2-2.5kg, 53% were 2.5-3kg and 4% were more than 3 kgs.

APGAR at the time of delivery: 92% were with APGAR 10 and 8% were with APGAR 8-10.

Causes for neonatal morbidity: Out of 54, 2 babies suffered with acute diarrhoea, 2 suffered with oral thrush and 1 with birth asphyxia and all of them had physiological jaundice.

Incidence of HIV seropositivity in children born to HIV positive mothers: Out of 54 babies 2 babies were not brought for follow up at 6 weeks and out of 52 babies, 1 baby is positive at 6 weeks and 51 babies are negative.

Transmission rate of HIV and efficacy of ART: Out of 54 babies who are given Nevirapine drops, only one baby became HIV positive, so the efficacy of ART is 98.04%.

ORIGINAL ARTICLE

DISCUSSION: HIV transmission from mother to child can occur during antenatal, intrapartum and post-partum periods.

HIV testing: Most people infected with HIV develop specific antibodies within three to twelve weeks of the initial infection. Diagnosis of primary HIV before seroconversion is done by measuring HIV-RNA or p24 antigen. Positive results obtained by antibody or PCR testing are confirmed either by a different antibody or by PCR.

Antiretroviral Therapy: Antiretroviral therapy (ART) is the use of HIV medicines to treat HIV infection. ART is recommended for everyone infected with HIV. The time to start ART depends on a person's unique needs and circumstances. ARV drugs belonging to 3 classes have been introduced and large number of others is under development. These are Nucleoside Reverse Transcriptase Inhibitors (NRTIs), Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs) and Protease Inhibitors (PIs). NRTIs include the drugs like Zidovudine, Didanosine, Lamivudine, Stavudine. NNRTIs include Nevirapine and Efavirenz. Protease Inhibitors include Indinavir, Nelfinavir, Ritonavir.

Whenever treatment is instituted, it should be aggressive (HAART) aiming at suppressing plasma viral load to undetectable levels (Less than 50 copies of HIV-RNA/ml). Therapy with 3 antiretroviral drugs is commonly used. Due to availability of multiple drugs, a variety of combination regimens is possible and has been employed. However, no specific combination can be considered optimal initial regimen for all patients. The most commonly employed initial regimens are:

- 2 NRTIs+1 PI
- 2 NRTIs+1 NNRTI
- 3 NRTs.

Nevirapine is a NNRTI which directly inhibits HIV reverse transcriptase without the need for intracellular phosphorylation. It is more potent than Zidovudine on HIV-1. Nevirapine is well absorbed orally and is extensively metabolized in liver with t_{1/2} of 30 hours. It induces CYP450 enzymes and enhances its own metabolism as well as other drugs. It is indicated in combination regimens for HIV and has succeeded in reducing HIV-RNA levels when an earlier regimen has failed. It is a cost effective.

Pregnant woman identified as HIV positive during antenatal check-ups were started ART irrespective of CD4 count. According to WHO guidelines ART can be initiated even in first trimester of pregnancy with HAART.

During antepartum period 25% to 35% of total transmission occurs mainly in the late pregnancy. The antepartum transmission can be managed by giving ART which reduces perinatal transmission and reduces the risk of drug resistance. The recommended regimen is based on two NRTIS (nucleoside reverse transcriptase inhibitor) plus an NNRTI (Non-nucleoside reverse transcriptase inhibitor) or boosted Protease inhibitor.

Recommended regimen is Tenofovir (TDF) 300mg+ Lamivudine (3TC) 300 mg single FDC pill /day+Efavirenz (EFV) 600 mg one pill/day. ART should be continued throughout the pregnancy, delivery and life long.⁽⁹⁾

During intrapartum 70% to 75% of total transmission occurs. The postulated mechanism is micro transfusion from constant massage of placental bed due to uterine contractions and exposure of baby's mucocutaneous surface to maternal blood and cervical secretions. Factors like vaginal delivery, prolonged contact with maternal blood during delivery, prolonged rupture of membranes,

ORIGINAL ARTICLE

chorioamnionitis, procedures that increase exposure of infant to maternal blood like instrumentation during delivery, episiotomy are associated with increased risk of transmission. Prematurity is a risk factor for increased transmission due to thin skin, susceptible mucous membranes, immature immune function and low level of maternal antibodies in the premature infant.

During intrapartum period a single dose of NEVIRAPINE at the onset of labour and a single dose of Nevirapine to the new born infant is an effective alternative therapy for women who had no prior ARV therapy. Nevirapine decreases the risk of transmission by two mechanisms- by reducing the viral load in the mother and by preventing the virus from fixing itself in the infant.

Pediatric virology committee of AIDS clinical trial group in the UNITED STATES has proposed definitions for determining inutero versus intrapartum transmission. It is considered that a child with a positive PCR within 48 hours of birth has been infected in utero and a PCR negative at 48 hrs. but positive 7 to 90 days after delivery indicates an intrapartum infection.

After delivery breast feeding accounts for 5% to 15% of total transmission. The risk varies depending upon the duration of breast feeding, associated breast abscess, cracks in nipples, mastitis and mixed feeding.

Avoidance of breast feeding, HAART therapy and appropriate mode of delivery has reduced MTCT rates from 25% to 30% to less than 1%.

Earlier options for preventing MTCT were limited but now the emergence of HAART has revolutionized the field of prevention strategies in mother to child transmission. This study was therefore, undertaken with the aim to evaluate the efficacy of ART in the prevention of mother to child transmission of HIV-1 infection.

In our study 54 babies born to HIV positive mothers, 51 were tested negative, one tested positive and 2 babies were not brought for follow-up. The mother to child transmission rate was found to be 1.96% and efficacy of nevirapine was 98.04%. Average birth weight of babies born to them was between 2.5 to 2.8 kg.

Reducing mother to child transmission of HIV from an early infant diagnosis programme in south region of Nigeria done by Chukuwumeka Anoje- two thirds of mother baby pairs received ARV and babies never were breast fed, transmission rate of for mother baby pairs who received ARVS for PMTCT was 4.18% at zero to 6 weeks of age compared to 19.5% when either baby nor mother received an intervention. Regardless of intervention, the transmission rates for babies aged 6 wks to 6 months who had mixed feeding was 25.6% whereas transmission rates for those who were exclusively breast fed was 11.8%.

In INDIA, MTCT rates of 48% have been reported by KUMAR et al and 36% by DONGAONKAR et al. Recent survey done in MAHARASTRA has shown seropositive rate 0.25% to 4%.

MATIDA in his study rate of perinatal transmission among babies born to HIV positive mother fell from 16% in 1995 to 2.4 in 2002 with intervention.

McCONNELL in 2007 conducted study with Sd NVP intervention, the rate of transmission was 11.3%.

CONCLUSION: The prevalence of HIV in INDIA is of great concern. Every antenatal woman should be tested for HIV, counseling should be given to improve the access of PPTCT services. The woman should be given the various intervention strategies available to prevent MTCT of HIV. With appropriate care and medication women living with HIV can expect a normal pregnancy and child birth.⁽¹⁰⁾

ORIGINAL ARTICLE

Reduction of MTCT of HIV is possible with effective interventions including improved access to ARVS and appropriate infant feeding practices. Loss to follow up of HIV exposed infants is a challenge and requires strategies to enhance retention.

The use of SdNVP to mother and child is associated with good efficacy in preventing MTCT of HIV. Along with single dose nevirapine infants should be given nevirapine prophylaxis.

Birth weight(gm)	NVP daily dose(mg)	NVP daily dose(ml)	Duration	Side effects of NVP
<2000gm	2mg/kg once daily	0.2 ml/kg once daily	Up to 6 weeks irrespective of exclusive breast feeding or replacement feeding (may be extended till 12 weeks if mother has not received ART For adequate duration)	Common: nausea and diarrhea Severe and rare: skin rash, mucosal involvement, jaundice and fever.
2000-2500 gm	10mg daily	1 ml once daily		
More than 2500 gm	15mg once daily	1.5 ml daily		

No. of Patients screened	No. of HIV sero positive cases	Rate incidence/ 100 women
7100	65	0.91%

Table 1: Incidence of HIV seropositivity

Fig. 1: Status of HIV Positivity in Pregnant women (0.91%)

Age group	No. of cases	Percentage
18-20	38	70%
21-25	14	26%
26-30	2	3.7%
More than 30	nil	0

Table 2: Age incidence in 54 positive women

ORIGINAL ARTICLE

Gravid state	No. of cases	Percentage (%)
Primi	38	70%
Second	14	26%
Third	2	3.7%
Four or more	NIL	0

Table 3: Gravid status in 54 HIV positive women

Fig. 2: Gravid status in 54 HIV positive women

Term Delivery	51	94%
Preterm Delivery	3	6%

Table 4: Gestational age at the time of delivery

Normal Vaginal delivery	46	85%
By LSCS	7	13%
Indications- 1. Failure to progress	2	
2. Foetal distress	2	
3. CPD	2	
4. Post Caesarian	1	
Instrumental Delivery – Outlet forceps	1	2%

Table 5: Mode of delivery

Less than 2 Kg	3	6%
2 – 2.5 Kg	20	37%
2.5 – 3 Kg	29	53%
More than 3 Kg	2	4%

Table 6: Birth weight of Babies

ORIGINAL ARTICLE

Fig. 3: Birth weight of Babies

8-10	4	8%
10	50	92%

Table 7: APGAR at the time of delivery

Birth asphyxia	1
Acute diarrhea	2
Physiological Jaundice	54
Oral thrush	2

Table 8: Causes for neonatal morbidity

	0 Days	6 Weeks	Percentage (%)
No. of Children tested	54	52	96.2
No. of Children became negative	53	50	96
No. of Children become positive	1	1	2
No. of children not brought for follow up	2	2	

Table 9: Incidence of HIV seropositivity in children born to HIV positive mothers

No. HIV Parturient	No. HIV positive infants	Transmission rate	Efficacy of ART
54	1	1.96%	98.04%

Table 10: Transmission rate of HIV and efficacy of ART

Fig. 4: Transmission rate of HIV and efficacy of ART

Fig. 5: HIV VIRION

REFERENCES:

1. Townsend CLC, Cliffe SS, Tookey PAP. Uptake of antenatal HIV testing in the United Kingdom: 2000-2003 ; 28: 248-52.
2. NACO document. (Last cited on 2010 Jan 21). Available from <http://www.nacoonline.org//NATIONALAIDSControlProgram/Servicesforprevention/IntegratedcounsellingandtestingICT>.
3. Singh AE, Lee B, Fenton J, et al. The INSTI HIV-1/HIV-2 antibody test: a review. Expert opin Med Diagn. 2013; 7: 299-308.

ORIGINAL ARTICLE

4. Khan AW, Bull L, Barton S. Management of HIV infection in pregnancy. *Obst Gynaecol Reprod Med.* 2013; 23: 1-6.
5. Williams I, Churchill D, Anderson j et al. British HIV association guidelines for the treatment of HIV-1 positive adults with antiretroviral therapy 2012. *HIV Med.* 2012; 13 (Suppl 2): 1-85.
6. Book: NACO guidelines for prevention from Parent to child transmission of HIV.
7. NACO document (Last cited on 2010 Jan 21). Available from: <http://www.nacoonline.org/miscellaneous/Prevention of Parent to Child Transmission/>
8. Bugard M, Blanche S, Jasseron C, et al. Performance of HIV-1 DNA or HIV-1 RNA tests for early diagnosis of perinatal HIV -1 infection during anti-retroviral prophylaxis. *J Peditr.* 2012; 160: 60-66. e 1.
9. Kokeju A, Handrahan Carshall N, et al. Revised National PPTCT Guidelines. Normalising childbirth in women living with HIV: a London teaching hospital experience. *Fetal Neonat,* 2012; 97; A116.

AUTHORS:

1. L. Jhansi Rani
2. G. Vanaja
3. Helena Bandi
4. Divya Shravani Kamedini

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Obstetrics and Gynaecology, Andhra Medical College, Visakhapatnam, Andhra Pradesh.
2. Assistant Professor, Department of Obstetrics and Gynaecology, Andhra Medical College, Visakhapatnam, Andhra Pradesh.

FINANCIAL OR OTHER

COMPETING INTERESTS: None

3. Post Graduate, Department of Obstetrics and Gynaecology, Andhra Medical College, Visakhapatnam, Andhra Pradesh.
4. House Surgeon, Department of Obstetrics and Gynaecology, Andhra Medical College, Visakhapatnam, Andhra Pradesh.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. G. Vanaja,
Door No. 9-7-289, Sairamnagar,
Lane besides O-Optex Showroom,
Gajuwaka, Visakhapatnam-530026,
Andhra Pradesh.
E-mail: vanajasekhar@yahoo.com

Date of Submission: 18/05/2015.
Date of Peer Review: 19/05/2015.
Date of Acceptance: 01/06/2015.
Date of Publishing: 06/06/2015.