

Neverapine drug regimen investigation on HIV mother to child transmission in Warangal (A.P.), India

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All over India out of about 28 million deliveries occur annually, 84,000 deliveries occur in HIV positive woman. Out of these 30-45% babies is getting infected by HIV. In states like Andhra Pradesh HIV prevalence is more than 1%. In Andhra Pradesh so far HIV has infected 4 lakh people. The most prevalent district in A.P. is Warangal. According to 2002 Ante natal clinic cases highest positive infection rate is 6.75%, STD clinic 40.40%. The great majority (90%) of HIV positive children acquired the virus from their mother. Reduction of mother to child transmission is therefore very important in India. Pregnant women from rural and urban areas visit Govt Maternity hospitals in Warangal and Hanamkonda for regular check up from 3rd month till delivery. When they visit, with their informed consent they would be screened for HIV antibody in the hospital settings. Out of total 287 HIV +ve women, 166 were pregnant women. 145 pregnant mothers were orally given nevirapine 200mg at the on set of labour and the new born babies were given 2mg/kg Neverpine syrup within 72 hours after delivery. 21 of the pregnant woman 16, 20, 28, week gestational age undergone medical termination of pregnancy. 60 of the nevirapine treated mothers and their babies came to the follow up. Follow-up mothers and their babies screened for HIV antibody in their blood, 18 babies are HIV antibody negative, 42 babies are HIV antibody positive out of this 15 Babies died due to unknown reason. Present studies show that in nevirapine drug treated HIV mother to child cases the Transmission reduction rate is 11% or above in Warangal, AP. Long term study on reducing vertical transmission of HIV infection is necessary. International and National organizations and NGOs should provide free baby food for sero negative infants born to HIV + mothers. Present study strongly suggests that the role of humoral and cellular responses provided through a breast milk is required to be investigated.

Key words : HIV prevalence, Transmission, HIV-tridot, Nevirapine, Labour, Cellular responses.

INTRODUCTION

GLOBALLY an estimated 65 million people had been infected with HIV, 25 million had died and 40 million are living with HIV/AIDS. Every day 14000 people are infecting with HIV/AIDS world wide. Presently 3.82 to 4.58 millions are infected in India. In Maharashtra, Tamilnadu, Karnataka, Andhra Pradesh, Nagaland and Manipoor infection rate is over 1% in antenatal clinics. In Andhra Pradesh 4 lakh people are infected with HIV. The most prevalent district in A.P. is Warangal. According to 2002 ANC cases highest positive infection rate is 6.75% and STD clinic is 40.40%. This is very high when compared with national data. The great majority of HIV positive children acquired the virus from their mother. 90% of infected children live in sub Saharan Africa and south East Asia. HIV transmission rate from mother to child is ranging from 25% to 40% in less developed countries and from 15% to 25% in more developed countries. Risk of transmission is affected by factors related to the virus, the mother, the delivery process, the baby and how the infant is fed. All these factors explain the differing rates of HIV transmission between more developed and less developed countries. During pregnancy and delivery the mother's health, disruption of the placental barrier, preterm delivery and hemorrhage are significant predictors of the child's infection. An estimated one out of every seven infants breastfed by an HIV positive mother becomes infected through milk.

MATERIALS AND METHODS

Pregnant women from rural and urban areas visit Maternity hospital for regular checkup from 3rd month till delivery. They were screened for HIV antibody in the hospital settings at these visits with an informed consent. HIV/AIDS testing lab and counseling room at this hospital were well established. Pre test

counseling and post-test counseling were performed. During April 2002 to March 2003 HIV positive pregnant mothers were encouraged to enroll for prospective study. Mother to Child HIV Transmission centers in maternity hospitals of Warangal is also well established. MTCT (mother to child HIV transmission) centers were provided with a gynecologist, a pediatrician, a physician, and a counselor. One of the authors with the help of the counselor interacted with HIV +ve patients with established questionnaires.

The infected mothers visited hospital at the 16 weeks, 20 weeks, 28 weeks, 36 weeks of pregnancy for their routine check up and finally for delivery. During one of their visits they were screened for HIV antibody. Pre test counseling was performed for all but post test counseling performed only for HIV infected women, during 16 weeks, 20 weeks, and 28 weeks of pregnancy; HIV infected mothers counseled for MTP (medical termination pregnancy). 4 – 5 ml peripheral blood is collected intravenously from 28, 36 weeks gestation period pregnant mothers who had taken Nevirapine drug treatment and screened for HIV-1/2. The sero positivity was confirmed by three individual tests. 1) HIV TRIDOT 2) NEVA TEST. 3) COMBAIDS or EIA (Enzyme immuno assay).

HIV TRIDOT

HIV tridot is a rapid test developed and designed using gp41, C-terminal of gp120 and gp36 representing the immuno dominant region of HIV-1 and HIV-2 envelop gene structures respectively. The HIV tridot test is a visual, rapid, sensitive and accurate immuno assay for the differential detection of HIV-1 and HIV-2 antibodies in human serum (or) plasma using HIV-1 and HIV-2 antigens immobilized on an immuno filtration membrane. The test is a screening test for anti HIV-1 and HIV-2 and *in vitro lab* use.

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NEVA (NAKED EYE VISIBLE AGGLUTINATION)

In NEVA test kit comprises of a set of several recombinant molecules. All these molecules have RBC binding sites. Such Universal RBC – Protein –binding sites have been selected. The molecules are so designed that each molecule has only one RBC binding molecules that contain fusion proteins, which are RBC binding molecules with different immuno dominant HIV antigenic regions fused at the other end these fusion proteins capture one arm of the anti HIV antibodies .

COMB AIDS – R

It is an *in vitro* visually read DOT immunoassay intended for the qualitative detection of Ig-G/Ig-M antibodies to the HIV type 1 &2 in human serum (or) plasma. A Comb AIDS employs the principle of enzyme immunoassay. In this test a positive result is indicated by the presence of magenta red colored dot on the surface of the Comb where peptides have been spotted.\

NEVIRAPINE

Nevirapine is non-nucleoside reverse transcriptase inhibitor that has potent antiviral activity. It is rapidly absorbed when given orally, and passes quickly through the placenta. The drug has long half life in pregnant women and babies.

Median 61-66 hours in pregnant women, after single 200 mg dose during labour and 45-54 hours in babies. 200 mg of nevirapine is routinely administered to seropositive pregnant women at on set of labour, while one dose of 2 mg/kg is given to baby within 72 hours after birth.

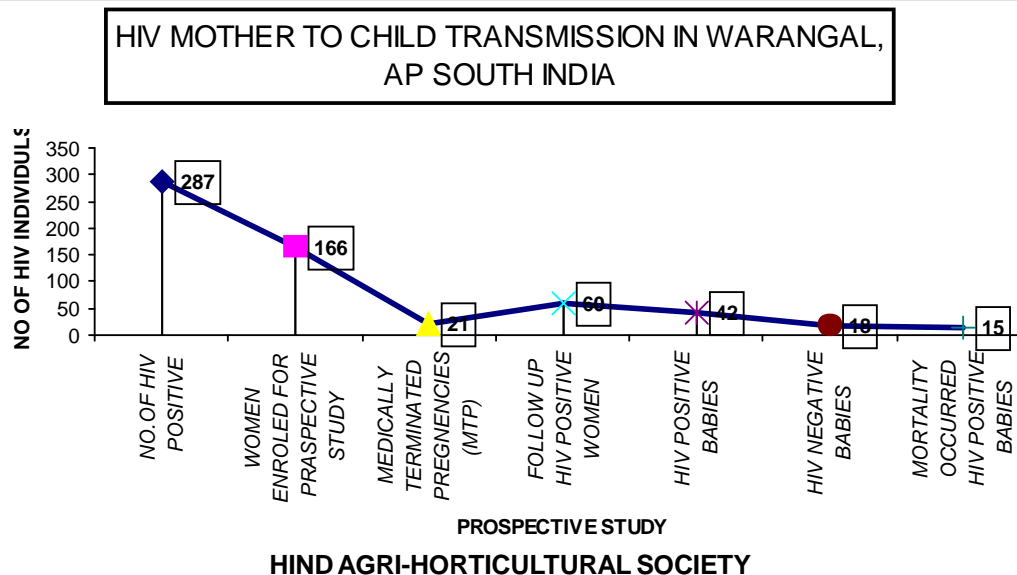
RESULTS AND DISCUSSION

Out of total 287 HIV +ve women, 166 were pregnant, 21 of the pregnant woman 16, 20, 28, week gestational age under gone medical termination of pregnancy. 145 pregnant women were orally given 200mg of nevirapine on set of labour and 2mg/kg never pine syrup was given for baby with in 72 hours after delivery. Immediately no screening test was performed and they were asked to come after 12 to 18 months. Antigen detection technique like PCR (polymerase chain reaction) is not available in this setting. During the 12 -18 months period, all the babies are breastfed. 85 navirapine drug study mothers and their babies did not come for the follow up. 60 of the nevirapine treated mothers and their babies came for the follow up. Follow-up mothers and their babies were screened for HIV antibody in their blood, 18 babies are HIV antibody negative and 42 babies are still positive Out of these 15 babies died due to unknown reason. Most of the babies and their parents came from remote rural places. They were not interested to come for follow up. Present studies show that HIV transmission from HIV mother to

child in nevirapine treated transmission reduction rate is only 11%.

All over India out of about 28 million deliveries occur annually, 84,000 deliveries occur in HIV positive woman. Out of these 30-45% babies are getting infected HIV. In states like Andhra Pradesh HIV prevalence is more than 1%.HIV can infect during gestation period, delivery, postnatally via breastfeeding. The foetus can be infected *in utero* through maternal blood, transplacental hemorrhage, umbilical cord and gastro intestinal route. Maternal secretions with blood, viral load, malnutrition, chorioamnionitis, instrumentation during delivery, feeding in the presence of cracked nipples or mastitis, prolonged breastfeeding are also causes for HIV infection. The vertical transmission of HIV through breast milk ranges between 16-29%. 30%of the babies who get infected vertically as follows 2% in early gestation, 3%in late gestation, 15% during labour, 5%in early post partum period 5% in late post partum period. Nevirapine drug regimen reduced mother to child transmission in Warangal, A.P., south Indian set up is 11% or above because so many rural navirapine drug regimen study mothers and their babies are not came follow up and their identification is also very difficult. Most of the women go to their villages of residence and few HIV infected mothers wrong address or changed their address due to some social discrimination. Most of the women are illiterate and their relatives are discouraging for the follow up. Few study group mothers and their babies also visit private clinics. In other parts of the world navirapine regimen has been extensively studied. Nevirapine reduced mother to child transmission in HIVNET 012 trail in Uganda 15.7%and SAINT trail in south Africa 12.3%DITRAME plus ANPS1201.o trail Abidjan, cot. D. Ivory 4.6% NVAZtrail Malawi 15.3%.

In developed countries long course of AZT is available and affordable but in developing countries it is not .In the early days of the infancy, diarrhea and respiratory problems are very common in the inmuno compromised infants. In developing countries like India most of of the pregnant women suffer from malnutrition and micro nutrition and babies born with low birth weight are vulnarable to various diseases. Breast feeding there fore is a must, so current WHO/UNAIDS/UNICEF guidelines recommended that women with HIV infection should be fully informed of both the risks and benefits of breast feeding practices In this setting poor remote pregnant women will come to the hospital only for delivery and more over they are not aware of their HIV status before arrive to the hospital. In HIV infected mother cell-associated and cell-free virus detected in breast milk. Colostrum has shown to have higher viral loads as also higher anti bodies levels. Few cellular and humoral factors are found to be reduced HIV transmission in colostrums samples



obtained from HIV seropositive mother as compared to seronegative mothers.

Breast-feeding offers infants' adequate nutrition protects them against some infectious diseases during the first six months of life, and greatly reduces the risk of gastrointestinal infections from contaminated foods.

Nevirapine causes fatal hepatotoxicity includes fulminant and cholestatic hepatitis, hepatic necrosis, and hepatic failure, during pregnancy combination of anti retroviral treatment causes pre term delivery Most of the ART are possible teratogenic agent Limitations of nevirapine induced drug toxicities in this set up are not studied. Present study strongly recommends that investigation of humoral and cellular responses in breast milk and sero negative infants who are born to HIV positive mother is also important for understanding this future epidemic. Strengthening the MTCT study in molecular level with the help of established laboratory, strengthening AIDS awareness programs in urban slums and rural parts is essential. Long term study on reducing vertical transmission of HIV infection is necessary. International and National organizations and NGOs should provide free baby food for sero negative infants born to HIV + mothers. Reducing the cost of anti retroviral drugs is also principally needed.

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