Effectiveness Of Interventions Among HIV Reactive Pregnant Women (In Andhra Pradesh)

A.K. Mishra*, E. Sowmya**

*Associate Professor, Department of Community Medicine, **Third year MBBS, Mediciti Institute of Medical Sciences Ghanpur, Medchal Mandal, Ranga Reddy Dist, 501401, Andhra Pradesh, INDIA

Abstract: Background: Over the years, single dose Nevirapine has been the cornerstone of the PPTCT program in India. However after successful scale up of ART program, initiation of ART for the pregnant was also considered another means of reducing the risk of transmission of HIV. As there were no specific studies to demonstrate the advantages of full-course ART during pregnancy compared to single dose Nevirapine, the current study was undertaken. Objectives: To study the socio-demographic variables, effectiveness of the different interventions and factors affecting the interventions among the PPTCT program beneficiaries.
Materials and Methods: As part of the retrospective cohort study the details of the HIV positive pregnant women registered at four ICTCs of Andhra Pradesh were analyzed in two groups (Nevirapine and ART).
Results: Total 145 pregnant women were studied and among them, 3.4% opted for MTP, 66.2% had live-birth and 60% had normal vaginal delivery. Upon testing for HIV at 18 months, 35% babies were HIV reactive in the Nevirapine group, 17.6% babies were HIV reactive in the ART group. Interpretation & Conclusion: The findings from the present study showed higher protection among babies with mothers on ART before delivery, compared to those with single dose Nevirapine. [Mishra A K et al NJIRM 2013; 4(2) : 26-31]
Key Words: Andhra Pradesh, ART, Effectiveness, Nevirapine, PPTCT Program, Retrospective Cohort study

Author for correspondence: Ms. E. Sowmya, III Yr, MBBS student, Mediciti Institute of Medical Sciences Ghanpur, Medchal Mandal, Ranga Reddy Dist, 501401, Andhra Pradesh. Email: sowmyasuperstar@yahoo.co.in

Introduction: Most children living with HIV acquire the infection through mother-to-child transmission (MTCT), which can occur during pregnancy, labour and delivery or during breastfeeding. In the absence of any intervention the risk of such transmission is 15–30% in non-breastfeeding populations. Breastfeeding by an infected mother increases the risk by 5–20% to a total of 20–45% [1, 2]. The risk of MTCT can be reduced to fewer than 2% by interventions that include antiretroviral (ARV) prophylaxis given to women during pregnancy and labour and to the infant in the first weeks of life - obstetrical interventions including elective caesarean delivery (prior to the onset of labour and rupture of membranes), and complete avoidance of breastfeeding[2,3]. With these interventions, new HIV infections in children are becoming increasingly rare in many parts of the world, particularly in high-income countries.

Efforts towards Prevention of mother-to-child transmission (PMTCT) of HIV have been at the forefront of global HIV prevention activities since 1998, following the success of the short-course Zidovudine and single-dose Nevirapine clinical trials. In India it was first launched in 2002 by the National AIDS Control Organization (NACO) after pilot testing in 11 major hospitals. At present there are more than 4000 integrated counselling and testing centres across the country[4]. As part of the programme, counselling and testing services are being provided to the pregnant women in the Integrated Testing and Counselling Centres (ICTCs). Pregnant women who are found to be HIV positive are given a single dose of Nevirapine at the time of labour; their newborn babies also get a single dose of Nevirapine immediately after birth so as to prevent transmission of HIV from mother to child. This program provides one of the most effective means and the potential in combating new HIV infections. The prevention of mother to child transmission is of paramount importance in reducing paediatric HIV and total number of HIV infected patients as the development of the vaccine has not shown much scope and may eventually take longer time and resources. Apart from posing the burden of HIV positive children on society, mother to child transmission is causing a great social problem by producing orphans after the death of one or both parents due to AIDS.

The Joint Technical Mission on PPTCT (2006) estimated that out of 27 million annual pregnancies in India, 189,000 occur in HIV positive pregnant women. In the absence of any intervention, an estimated cohort of 56,700

infected babies will be born annually. The PPTCT services cover about 10% of pregnancies in the country. In the year 2006, 2.1 million pregnant women accessed this service. Of these, more than 16,500 pregnant women were HIV positive. In order to provide universal access to these services further scale up is planned up to the level of Community Health Centre and the Primary Health Centre, as well as private sector by forging public-private partnerships. Through these measures NACO hopes to achieve the United Nations General Assembly Special Session (UNGASS) target of reducing the proportion of infants infected with HIV/AIDS by 50 percent by 2010[4]. Although there have been many alternative regimens being implemented all over the world as part of this program, NACO has been advocating and implementing the single drug (Nevirapine) administration in the country's program from the beginning.

However to improve the efficiency of the intervention, in recent years NACO has proactively started promoting the initiation of ART (Antiretroviral Therapy) among the eligible pregnant women so that the viral load can be brought down significantly and the risk of transmission can be minimized further.

Materials And Methods: A retrospective Cohort study was carried out in four selected Integrated Counselling & Testing Centres (ICTCs) of Hyderabad district. To start with, all the ICTCs in Hyderabad and Ranga Reddy districts were listed and their caseload was analyzed with the help of the data from the Andhra Pradesh State AIDS Control Society Annual report and four of the reasonably high case load centres were considered for our data collection. All the HIV positive pregnant women registered between January 2007 and December 2008 in these ICTCs were considered for the project. They were followed till the outcome of the pregnancy and in case of live birth, the mother-baby pair was followed till 18th months for HIV testing. The cohort study was done to assess the outcome of pregnancy and in case of live birth the confirmed HIV status of the baby at 18 months of age. For this, four major ICTCs were chosen; Osmania Maternity Hospital, Gandhi Hospital, Niloufer Hospital and Mediciti Hospital. The data regarding the pregnant women registered at these centres was collected and recorded in the ICTC registers during the time of counselling sessions with written consent from the beneficiaries. Necessary permission was obtained from the Deputy Director General, (Monitoring & Evaluation), National AIDS Control Organization, New Delhi for accessing the data available in the records as well as carrying out the study. A total of 3 months was utilized for completion of this project.

An attempt was made to include all the HIV positive pregnant women from these ICTCs. Keeping the fact that less number of pregnant women were put on ART during pregnancy between 2006 and 2008, who would have completed 18 months for getting the confirmed status of HIV infection among their babies, a purposive sample size of 100 was considered adequate. Among the 100 pregnant women, 50 mother-baby pairs who were administered only with Nevirapine as part of the PPTCT intervention were considered as one group and rest of the 50 pregnant women who were put on ART were considered as part of a different group. A format was developed for collecting the information about the variables from the available records and registers in the selected ICTCs, which included the variables for determining the factors affecting the intervention.

Independent variables: Socioeconomic status of the pregnant women & their spouses, gravida & parity, ART status, duration of ART, Nevirapine administration to mother & baby, type of delivery and breastfeeding pattern.

Dependant variable: HIV status of babies at the completion of 18 months.

Brief procedure: The ICTCs in the districts of Hyderabad and Ranga Reddy districts were listed and depending upon approachability and accessibility, four major ICTCs, Osmania Maternity Hospital, Gandhi Hospital, Niloufer Hospital and

Mediciti Hospital were finalized. A format was developed to collect the information about the variables. Each of these four hospitals was visited and necessary permission was obtained from the concerned authority to collect the information from the existing medical records of the ICTCs. Utmost care was taken to maintain confidentiality of the information collected through this study. No personal information regarding the name, residence, contact details was collected about the study participants.

Statistical Analysis: Data was entered in MS Excel. After data cleaning and validation, it was analyzed using Epi Info. The mean, standard deviation, proportions were calculated for categorical variables. Bivariate analysis was done using Fisher Exact Test for assessing the association between the independent and the dependent variables and "P" value was calculated. "P" value was considered significant if it was <0.05.

Ethical considerations: There was no direct data collection from the beneficiaries, and none of the beneficiaries were involved in any additional interventions. Written consent was taken from the participant at the time of Pre-test counselling in the ICTCs and for using the already collected data from the registers necessary approval was obtained from the Deputy Director General (Monitoring & Evaluation), National AIDS Control Organization (NACO), New Delhi. Also there was no issue of human rights violation involved in the study. The study proposal was first presented before the Institute Research Council. Following its approval along with the permission from NACO, necessary approval was also obtained from the Institute Ethics Committee. There were no conflict of interest of any sort for this study.

Result: During the study period, data for 145 pregnant women could be collected from the above mentioned four ICTCs, who satisfied the inclusion criteria. The mean age of the participants was 22.7+3.07 years.

Among the studied population, 24 (16.6%) were illiterates, 6 (4.1%) had studied up to primary class, 12 (8.3%) had studied up to secondary class and 4 (2.7%) had studied higher secondary and above. There was no data available for 99 (68.3%) of them regarding educational status.

Among the 145 women, 47 (32.4%) were housewives, 3 (2.1%) labourers, 3 (2.1%) were employed and no data was available for 92 (63.4%) pregnant women regarding occupation.

Among the pregnant women 55 (37.9%) were put on ART before delivery, 33 (22.8%) women were primigravida, 48 (33.1%) were 2nd gravida and 22 (15.1%) of them were 3rd gravida or above.

Analysis of gestational age showed that 20 (13.8%) had registered in the first trimester, 27 (18.6%) in 2nd trimester and 47 (32.4%) in 3rd trimester.

Of the 29 spouses whose age particulars were available, the mean age was found to be 28.5+4 years. Among them 14 (9.7%) were illiterates, 5 (3.4%) had studied up to primary level, 10 (6.9%) had studied up to secondary level and only 2 (1.4%) had studied beyond secondary level. Educational status of 114 spouses was not available in the registers. Among the 104 spouses whose data was available in the registers regarding HIV status, 67 (46.2%) were found to be HIV reactive and 35 (24.1%) were HIV nonreactive, one had died and one was not tested for HIV. Among the 67 HIV reactive spouses, only 6 were on ART.

Among the 145 pregnant women, 5 (3.4%) had opted for MTP. Among the rest 140 pregnant women who had undergone delivery, 96 (66.2%) of them had live birth, 10 (6.9%) had stillbirth and remaining 34 (23.4%) had no information about their outcome of pregnancy. Among those who underwent delivery, 24 (16.6%) had normal delivery, 14 (9.7%) had caesarean section, 2(1.4%) were delivered through assisted delivery and rest 100(71.4%) had no information available about type of delivery. Among the studied population, 103 (71%) pregnant women received single dose Nevirapine tablets just before delivery and 94 (64.8%) babies received single dose Nevirapine syrup immediately after delivery. The data

regarding administration of Nevirapine was not available for 33 (22.8%) mothers and 38 (26.2%) children.

Overall 91 mother-baby pairs received Single dose of Nevirapine. Exclusive breastfeeding was given to 25 (17.2%) babies and same number of them also received artificial formula feeding.

Total six (4.1%) received mixed feeding during infancy. The data regarding feeding pattern was not available for 89 babies. At the end of 18 months, 6 babies had died and 98 babies were lost to follow up. Among the remaining 41 babies, 11 (7.6%) babies were found to be HIV reactive and 30 (20.7%) were nonreactive. The studied population was divided into 2 groups one who received Nevirapine and the other group who were on ART. The mean age was 22.7 + 3 years for the women in the Nevirapine group and it was 22.6 + 2.9 years for the women on ART. The unpaired Independent T-Test analysis of the age of both the groups showed that the difference was statistically insignificant, justifying the comparability of the two groups.

Table 1: Showing the outcome of HIV testing for babies at 18 months

Variables (No.)	HIV Reactive (%)	HIV Nonreactive (%)
Type of Intervention		
Nevirapine (20)	35	65
ART (17)	17.6	82.4
Type of Delivery		
Normal Delivery (7)	28.5	72.5
Caesarean section (9)	22.2	77.8
Type of Feeding		
Exclusive Breastfeeding (6)	33.3	66.7
Artificial Formula Feeding (12)	17	83
Mixed Feeding (5)	20	80

Table-1 showed the distribution of outcome of testing of babies tested at 18 months based on type of intervention, delivery and feeding. Fisher Exact Test (as expected values for one of the cells was <5) was conducted for all the independent variables and the outcome of HIV testing for the babies at 18 months. Significant association could not be proved for any of the variables.

Table 2: Showing the outcome of HIV testing in the two intervention groups.

Interventions (No.)	HIV reactive (%)
ART + Caesarean section + No Breast Feeding (5)	0
Nevirapine+ Caesarean section + No Breast Feeding (5)	20

Discussion: The study was planned with a sample size of 100; however we were able to collect data for 145 pregnant women. After analysis we realized that the effective number came down to around 40, as for most of the variables the data were incomplete. Besides getting data for a research purpose from a programmatic setting is also a limitation. The registers in the programmatic setting are designed so as to facilitate the reporting about the program deliverables. The unavailability of complete data for all the eligible participants could be attributed to three major reasons. 1) The data was to be compiled from 4-5 sets of registers, first one having personal particulars and socioeconomic variables, the second one with details collected during the time registration and also containing details about delivery, third one having details about spouses, fourth one having details about children and their follow up till 18 months maintained at the ICTCs and finally the fifth one having the details in the ART registers. So the challenge was to link all the 5 registers, especially when it is manually maintained in hard copy registers. 2) It is also to be understood that as per Indian tradition most of the women prefer being at the mother's place for delivery and postpartum care. So those women, who are usually registered at one hospital for antenatal check up, may not necessarily deliver in the same hospital. Because of this also there was significant data gap noticed in our study. 3) The follow up period in this type of study was almost 3 years, from the time of registration of pregnancy till 18

months of babies' age, which was also a major cause of attrition and data gap. It is observed that most of the studies related to this topic have very small sample size. In the study by Parameshwari et al in Namakkal district of Tamilnadu, 56 HIV positive pregnant women were included and by the completion of 18 months only 14 babies could be tested for HIV and only 2 (14%) were found to be HIV positive. This study has shown protection of 86% by virtue of the single dose Nevirapine administration to mother-baby pairs. In our study we could get HIV test status of 37 babies at the end of 18 months and the protection achieved was 65% due to Nevirapine and around 82% due to ART[5]. In the study by Sukanta Mandal et al conducted in West Bengal, 34 babies were tested with single dose Nevirapine administration, out of which 10 (29%) were HIV reactive. However among the mother-baby pairs who received Nevirapine and the babies were given artificial feeding, showed a protection of 85% from the HIV transmission. The finding is corroborated by our study also as 83% protection was seen among the babies who were on exclusive artificial feeding[6].

Though in our study we have followed the babies till the completion of 18 months and tested them by routine antibody testing as done in the ICTCs, many studies have shown the results by just following the babies for 1-4 weeks and testing them by DNA-PCR. As already known, DNA-PCR may be a sensitive test for HIV, but not a very specific one. It is prone for high false positive rate. In the study conducted by Mark Colvin et al in South Africa, infants up to the age of 3-4 weeks were recruited and were tested by DNA-PCR.

Among 294 women who received Nevirapine as per the protocol, 29 (9.9%) babies were HIV reactive compared to 24 (13.4%) of the mothers who received the drug outside the time band (either too early or too late). Among the mothers who never received Nevirapine, 14.2% babies were found to be HIV reactive[7]. Theoretically it is understood that 3 drug ART regimen initiated during pregnancy would be definitely far better than administration of single drug (Nevirapine) to the pregnant women, but in practice it becomes really difficult to implement any alternate regimen. The challenges in a public health setting especially in a country like India with diverse cultural practices and varying degree of health system infrastructure, accessibility to affordable health care, literacy rate and socio-economic condition, full-fledged initiation of three drug regimen of ART for the HIV reactive pregnant women may take some more years. In the year 2006, the uptake of PPTCT program was just 10% for the whole country[4]. The program was being implemented mostly in the public sector. The recent initiatives made by NACO to involve more of private sector and take the program beyond Community Health Centre level in public sector hospitals, will bring more beneficiaries into its fold and simultaneously the ART services also must gear up in equally proportionate manner so as to meet the growing demand. An important link in this whole chain is the Laboratory support in terms of CD4 testing, which needs to be strengthened. The real challenge comes when the pregnant women after being diagnosed for HIV, finds it challenging to travel from the rural areas to the few designated CD4 testing centres which are currently functional. The blood sample transportation system needs to be supported till such time, the CD4 testing facility gets decentralized sufficiently. As the finding from our study were statistically insignificant due to relatively small sample size, in future there is scope of conducting large scale studies on this subject taking care of the limitation on a research set up.

Conclusion: A total of 145 pregnant women were followed in two cohorts as part of a retrospective cohort study conducted in four major ICTCs of Hyderabad district of Andhra Pradesh. The study cohort comprising the HIV pregnant women who were put on (3 drug regimen) ART during the antenatal period were compared with the control cohort of HIV positive pregnant women who were administered with single dose Nevirapine as per the NACO protocol. The babies from both the cohorts were tested at 18 months by routine antibody testing using 3 test kits as per the NACO protocol and found that 82% protection was seen among the babies in the ART cohort compared to 65% protection obtained in the Nevirapine cohort.

The protection offered by caesarean section (78%) was higher compared to that by Normal delivery (71%). Similarly the protection obtained by artificial formula feeding was 83% compared to exclusive breastfeeding which was 66%. The combined protection of artificial feeding and caesarean section with ART was 100% compared to that of 80% in Nevirapine group. However the findings were not statistically significant.

Acknowledgement: The authors are grateful to the Indian Council of Medical Research (ICMR) for providing necessary grant to conduct the study and to the Monitoring & Evaluation Division, National AIDS Control Organization (NACO), New Delhi for providing the required approval to use the available data. We are also thankful to the Mediciti Institute of Medical Sciences for granting necessary permission to carry out the study and issuing desired clearance through the Institute Research Board. We are pleased to acknowledge the valuable contribution by the higher authorities of the three other hospitals (Osmania Hospital, Gandhi Hospital and Niloufer Hospital) for providing access to their hospital data and concerned counsellors of the Integrated Counselling and Testing Centres (ICTCs) located in these hospitals for their timely support and excellent cooperation. Finally I would like to thank Dr. S. B. Rotti (Bangalore) for his valuable technical inputs on the article.

References:

1. De Cock KM, Fowler MG, Mercier E, De Vincenzi I, Saba J, Hoff E et al. Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice. Journal of the American Medical Association.2000 Mar 1; 283(9):1175–1182.

2. Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: Towards universal access. Recommendations for a public health approach. World Health Organization. 2006; Page-7.

3. Read J et al. A prospective cohort study of HIV-1-infected pregnant women and their infants in Latin America and the Caribbean: the NICHD International Site Development Initiative Prenatal Study. 12th Conference on Retroviruses and Opportunistic Infections. Boston, MA, USA. 2005 Feb 22-25 (Abstract 790).

4. National AIDS Control Organisation: Department of AIDS Control. Available from: http://www.nacoonline.org/National_AIDS_Control_Program/Services_for_Prevention/PPTCT/

5. Parameshwari S, Jacob MS, Vijayakumari JJ, Shalini D, Sushi MK, Sivakumar MR. A program on prevention of mother to child transmission of HIV at government hospital, Tiruchengode taluk, Namakkal district. Indian J Community Med 2009; 34:261-3.

6. Mandal S, Bhattacharya RN, Chakraborty M, Pal PP, Roy SG, Mukherjee G. Evaluation of the Prevention of Parent to Child Transmission Program in a Rural Tertiary Care Hospital of West Bengal, India. Indian J Community Med. 2010 Oct-Dec; 35(4): 491–494.

7. Colvin M, Chopra M, Doherty T, Jackson D, Levin J, Willumsen J et al. Operational effectiveness of single-dose Nevirapine in preventing mother-to-child transmission of HIV.
Bulletin of the World Health Organization. 2007 June; 85(6): 466-473.

8. Mother-to-child transmission of HIV infection in the era of highly active antiretroviral therapy. Clinical Infectious Diseases.2005 Feb 1; 40(3):458–465.

9. Dorenbaum A, Cunningham CK, Gelber RD, Culname M, Mofenson L, Britto P et al. Two-dose intrapartum/newborn Nevirapine and standard antiretroviral therapy to reduce prenatal HIV transmission: a randomized trial. Journal of the American Medical Association. 2002; 288(2):189–198.

10. Irene YV, Arun A. Efficacy of Single Dose Nevirapine in Prevention of Mother to Child transmission of HIV-1. J Obstet Gynaecology India (Vol. 60), No. 3: May - June 2010; pg 221-224.

11. Rajesh L, Ramesh K, Hanna LE, Narayanan PR, Swaminathan S. Emergence of drug resistant mutations after single dose nevirapine exposure in HIV-1 infected pregnant women in south India. Indian J Med Res. 2010 November; 132(5): 509-512.

Conflict of interest: None