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Research Article

PERINATAL OUTCOME IN HIV INFECTED PREGNANT WOMEN AT TERTIARY CARE HOSPITAL IN NORTH INDIA: ELEVEN YEARS RETROSPECTIVE STUDY

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ABSTRACT

Mother to child transmission (MTCT) of HIV is a major route of infection in children. Aim of this study was to know perinatal outcome in HIV infected pregnant women.
This retrospective study conducted from September 2005 to July 2016, carried at G.S.V.M. Medical College, Kanpur U.P. Hospital records of all HIV infected pregnant women and follow up details of babies were obtained. Out of 80 deliveries;65% delivered vaginally, 11 (13.8%) babies were still born and 14(17.5%) were neonatal deaths. 32.5% were low birth weight (LBW).All neonates received nevirapineprophylaxis. 55.2% preferred breast feeding. Four infants died and 2 babies turned HIV positive.
In our study, most common cause of perinatal mortality was prematurity, LBW and birth asphyxia. Overall MTCT rate of HIV was 3.4%. To conclude, transmission of HIV infection can be prevented by counseling, adequate antenatal care, antiretroviral therapy (ART) and simultaneously avoiding mixed feeding.

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INTRODUCTION

The first AIDS case was reported in 1981 and now it becomes a global pandemic. India has third largest number of estimated people living with HIV/AIDs. There are an estimated 21.17 lakhs people living with HIV/AIDS of which 6.54% are children (<15 years) with an adult prevalence of 0.26% in 2015. HIV prevalence has declined consistently over last one decade from 0.4% in the year 2000 to 0.26 in 2015. This decline reflects impact of scaled up HIV prevention interventions under the National AIDs control programme (NACP) through PMTCT services (NACO, GOI, 2006)[1].

According to HIV sentinel surveillance 2014-15 by the NACO, overall HIV prevalence is 0.29% among antenatal clinic attendees (NACO,GOI,2006)[1]. Young adults especially women of reproductive age group and children are mainly affected (Ezechi OC *et al*, 2013)[2]. Mother to child transmission of HIV is a major route of new infection in children (Shah NK, 2006; Kennedy D, 2012)[3,4,5]. More than 95% of HIV infection in children are due to vertical transmission (Shah NK, 2006)[4].20% transmission occur before 36 weeks gestation, 50% in the days before delivery and 30% intrapartum (Kourtis AP, 2001)[6]. Transmission rate for Breast feeding may be as high as 30-40% (Kourtis AP, 2007)[7]. Though children represent only 6% of the HIV infected population they contribute to one-sixth of HIV deaths (Shah NK, 2006)[3].

The association between maternal HIV status and pregnancy outcome was studied in Tanzania, and the HIV infected mothers were found to have a 75% higher risk of preterm delivery compared with the HIV negative mothers. The risk of perinatal death in the HIV infected group was found to be 89% higher than that in the non-infected group (Habib N, 2008)[8].

The early diagnosis of children born to HIV DNA-polymerase chain reaction (PCR) and treating children who are diagnosed HIV positive with anti-retroviral (ARV) drugs within their first 12 weeks of life reduces the mortality by 75% (Shah NK, 2006; Kennedy, 2012)[4,5]. Both maternal and fetal outcome can be improved by increasing awareness and effective implementation of PMTCT programme which includes HIV testing facility to all pregnant women with provision of ARV prophylaxis. This retrospective study was conducted to analyze the incidence of HIV transmission in children born to HIV infected pregnant women and neonatal outcome in past 11 years intertiary care hospital of northern India.

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MATERIAL AND METHODS

Location and duration of study

This retrospective study conducted from September 2005 to July 2016, carried out at G.S.V.M. Medical College, Kanpur U.P. Total 102 women were found seropositive for HIV infection. The hospital records of all HIV infected pregnant women were collected .Out of 102, 80 women delivered in our hospital, rest were aborted or lost to follow up. Data on demographic profile, mode of delivery and neonatal outcome were obtained and analyzed. For HIV positive women detected for the first time and for those who were not on ART during September 2005 to February 2014; single dose Nevirapine 200 mg were given during labour and 2 mg /kg to the neonate soon after the delivery. If she was already on treatment then ART was continued. From the year October, 2012 to July 2016 for HIV positive women ART (triple drug regimen- Tenofovir 300 mg, Lamivudine 300 mg and Efavirenz 600 mg) was started at 14 weeks of gestation or whenever she was diagnosed. Nevirapine 0.2 ml/kg/day was given to all babies from birth through age 4-6 weeks regardless of infant feeding method. Exclusive breast feeding was advised for all women.

Follow up of both mother and babies was done. Dry Blood Spot (DBS) of babies was done at 6 weeks, 6 months, 12 month and 18 months. Confirmation of HIV status was only at 18 months of age. All HIV positive babies were referred to ART center and ART was started according to NACO guidelines.

Statistical Analysis

Data analysis was done using simple measures like mean and percentage.

RESULT

Between September 2005 to July 2016, 34924 women were tested for HIV antibodies, out of which 102 women (0.3%) were found seropositive. Out of 102 seropositive women,6 women had spontaneous abortions, 5 women opted for MTP after counseling at gestational age less than 13 weeks, 4 women were lost to follow up, 4 delivered outside town and there were 3 antenatal mortality. Finally, 80 delivered in hospital, in which majority of women were in age group 21-30 years, multigravida (62.7%) and registered in third trimester (58.8%). Mean age of women was 25.2 years and mean parity was 1.6. Six (7.5%) women were neither on ART nor got Nevirapine prophylaxis. CD4 count of 35% women was less than 350 out of which 13.7% had CD4 count <200.52 babies (65%) were born by vaginal delivery and 28 (35%) by caesarean section (Table 1).

Table I Maternal Demographics (n-80)

Mean age	**25.2 years**
Mean parity	1.6
ART status / Nevirapine	
Yes	74 (92.5)
No	6 (7.5%)
CD4 count	
<200	11 (13.8%)
200-350	17 (21.2%)
>350	52 (65%)
Mode of delivery	
LSCS	28 (35%)
Vaginal	52 (65%)

Out of 80 deliveries, 77 were twin and rest singleton. Still birth were 11 (13.8%) and ultimately total live birth was 72. Early neonatal death was 10 (12.5%) and late neonatal death was 4 (5%) (Table 2).

Table II Perinatal outcome (n=80)

1.	**Total deliveries**	**80**
	Singleton	77
	Twin	3
2	Still birth	11
3	Total live births	72
4	Early neonatal death	10
5	Late neonatal death	4

The mean gestational age at delivery was 37.4 weeks.20 (25%) were preterm. 9 women (11.2%) had early preterm and 11(13.8%) had late preterm births. 60 women (75%) delivered at term. 17 were spontaneous. 3 were induced. Causes for preterm induction were PPROM in 2 patients and IUGR in one woman. 10 (12.5%) babies had very low birth weight. 16 (20%) had low birth weight and rest 54(67.5%) had appropriate weight for gestational age. In total 72 live births. 22 babies (30.6%) required nursery admission. Most common cause was prematurity, low birth weight (LBW) and birth asphyxia. All babies got Nevirapine prophylaxis. 32 out of 58 mothers (55.2%) chose to breast feed (babies who crossed the neonatal period). Among the 32 breastfed infants, 10 infants were breast fed for six months, rest were breastfed for variable periods from 2 months to 5 months and were switched to replacement feed (Table -3).

Table III Infant Demographics

1. **Gestational age (n=80)**	
<34	9 (11.2%)
34-37	11 (13.8%)
>37	60 (75%)
2. **Birth weight (n=80)**	
Very low birth weight	10 (12.5%)
Low birth weight	16 (20%)
>2.5 gm	54 (67.5%)
3. **Nursery admission (n=72)#**	
Yes	22 (30.6%)
No	50 (69.4%)
4. **Nevirapine prophylaxis**	
Yes	72 (100%)
No	0
5. **Feeding options (n=58)£**	
Breast feeding	32 (55.2%)
Replacement feeding	26 (44.8%)

Excluding still births
£ Excluding still birth + neonatal deaths

Table IV Maternal Profile of HIV-1 DNA PCR Positive Infants

	I	**II**
Age	24	28
Gravida	Primigravida	Primigravida
Habitat	Urban	Urban
ART status	Nevirapine prophylaxis	Nevirapine prophylaxis
CD4 count	447	417
Mode of delivery	Vaginal	Vaginal
Occupation of father	Private Job	Driver
Spouse status	Non reactive	Reactive
Gestation age	Term	Term
Nevirapine prophylaxis to baby	Given	Given
Gender	Male	Female
Mode of feeding	Mixed	Mixed

Fig-1 is showing detail follow up of babies. Out of 58 babies followed, 4 were lost to follow up and 4 died during follow up. At the end of 18 months follow up, 48 children were non-reactive and 2 were reactive. Both reactive children were referred to Pediatrics ART centre. Details of both PCR-positive infants are given in table-4.

DISCUSSION

In this 11 years retrospective study, 102 pregnant women were found seropositive. Mean age in this study was 25.2 years which is comparable to study done by Prameela *et al* (2015)[9] in which mean age was 23 years, while mean age was 30 years in study done by Ezechi *et al* (2013)[2]. In this study, 62.7% women were multigravida and mean parity was 1.6which is comparable to Ezechi *et al*[2] having mean parity of 1.7± 1.1 while in study by Prameela *et al*[9], 59.3% were primigravida. It is noticeable that majority of women got nevirapine prophylaxis, only 7.5% women were not on any ART/ARV prophylaxis which is less than study done by Prameela *et al*[9] and Malik *et al* (2015)[10] in which percentage was 10.2% and 16%.CD4 count <350 cells/µl was found in 35% women while in study by Kennedy *et al*[5]; 48.3% had CD4 count <350 cells/µl. Even 13.7% women had CD4 count less than 200 cells/µl, while in study done by Gautam *et al* (2016)[11], Malik *et al*[10], Prameela *et al*[9] and E.Azria (2014)[12] *et al* 15.4%, 24%, 26.9% and 12.6% women had CD4 count less than 200 cells/µl respectively. Most of the women delivered vaginally (65%) as in our hospital LSCS in HIV positive women is done for obstetrics indication only. Similarly in study done by Gautam *et al*[11], Prameela *et al*[9], Kale *et al* (2016)[13] and Ezechi *et al*[2]; 70.8%, 73.7%, 64% and53.1% women delivered vaginally respectively. In contrast to E. Azria[12] *et al* study 55% delivered by LSCS.

Total still births were 11 (13.8%) and the most common cause was prematurity and women who reported in advanced labour. Main causes of neonatal death were prematurity, birth asphyxia followed by septicemia. To conclude, most common cause of perinatal mortality was prematurity, LBW and birth asphyxia similar to study done in Tshwane South Africa (2010); where also both stillbirth and neonatal mortality rates were significantly higher for HIV positive mothers, with intrapartum asphyxia, preterm labour and infections were main contributing factors[14]. Ezechi *et al*[2] also demonstrated significant increase in perinatal death in HIV positive women and prematurity, low births were the leading cause of perinatal mortality. A review of the world literature suggests a clear association between HIV infection and still birth. A meta-analysis of 31 trials reported a fourfold increase in stillbirths if a group of mothers infected with HIV is compared with a similar group of mothers testing negative for HIV[15]. A smaller prospective study in Kenya, comparing perinatal outcome in a seropositive group of mothers with that in a matched seronegative group, found a significant increase in preterm birth in the seropositive group (21% v. 9.1%) and a small increase in perinatal mortality was also found in seropositive group[16]. Ellis *et al* (2002) also commented in their conclusion that seropositive mother was 'more likely to have a perinatal death'[17]. In Indian studies by GautamS *et al*[11] and Prameela *et al*[9]; still birth were less, 3.1% and 3.9% respectively in comparison to current study. Neonatal deaths (17.5%) were also more in comparison to study by Gautam *et al*[11] (13.8%).

In our study 20 women (25%) delivered preterm (<37 wks). Most common cause of preterm was PROM (75%). It is possible subclinical chorio-amnionitis may more common in HIV infected mothers and this could cause preterm labour and perinatal hypoxia[18,19]. Habib *et al* had also shown an association between maternal HIV status and preterm labour[8]. Preterm deliveries were 1.8% in study by Prameela *et al*[9], 4% by Malik *et al*[10], 13.1% by Ezechi *et al*[2] and 19% by Yudin *et al* (2016)[20]. but in our study preterm birth rate was 25% which was more than national average of approximately 21%[21].

In this study, 32.5% babies had low birth weight, while in study by Prameela *et al*[9] 49.2% babies had birth weight <2.5 kg. Ezechi *et al*[2]also found low birth weight was significantly higher in HIV positive women as compared to HIV negative women. While in study by Kennedy *et al*[5] and Kale *et al*[13], no significant difference was noticed in birth weight of babies between HIV exposed and negative groups. In study by GautamS *et al*[11]; all babies required NICU admission but only 1 baby stayed for more than 5 days and rest discharged within 5 days, while in our study 30.6% required nursery admission. 2.2% babies were not covered by Nevirapine prophylaxis in study by Prameela *et al*[9]. While allbabies got Nevirapine prophylaxis in our study and by Seenivasan *et al* (2014)[22].

Although exclusive breast feeding was advised, only 47.06% mothers exclusively breastfed the babies, which is less compared to Prameela *et al*[9] (65.2%) and Seenivasan *et al*[21] (60%). Rest 52.94% opted for replacement feed after counceling. Palombi *et al* (2007)[23] showed a transmission rate of <2% with alternatives to breast feeding without an increase in mortality in non breastfed group. Ezechi *et al*[2] noted that majority of the HIV positive women opted not to breastfeed after counseling on infant feeding options in context of HIV infection.

Fig. 1 is showing perinatal outcome and follow up of babies. Out of total 80 deliveries at hospital, live births were72. But only 58 babies followed, as 14 babies died in neonatal period. After18 months of follow up, 2 babies were found reactive. The overall parent to child transmission rate in this study was 3.4%, which was less when compared to study by Kale *et al*[13] (8.06%), Jacob *et al*[24] (8.3%) and Seenivasan *et al*[22] (4%). But more in comparison to Prameela *et al*[9] (1.8%) and Ezechi *et al*[2] (0.97%).This transmission rate was also less than the expected 10 to 20% in a pilot study done by NACO[3].

In our study details of both PCR positive babies is given in table 4. Both delivered vaginally, CD4 count of mother of both positive babies was >350 cell/mm^3 and both women were not on triple drug therapy but Nevirapine prophylaxis was given. Marazzi *et al* (2010)[25]also showed a transmission rate of 50.6% from mother with CD4 count >350 cells/mm^3 and these women were not on ART. Ugochukwu (2010)[26] *et al* found lower transmission rate when both mother and baby were on prophylaxis. So probable cause of MTCT in current study may be mixed feeding and both women were not on triple drug therapy.

Therefore, recent guidelines and several studies recommend triple drug regimens to prevent PTCT of HIV[27,28,29]. Single dose Nevirapine may also be associated with increase risk of resistance[30]. According to NACO also, PPCT triple drug

therapy should be given to all HIV positive pregnant females irrespective of their CD4 count and exclusive breast feeding should be continued for 6 month along with daily nevirapine.

Although previous studies[31,32,33] found an association between HIV infection in pregnancy and increased rates of low birth weight, prematurity, perinatal deaths, birth asphyxia and neonatal admission. In this current study also, incidence of preterm (25%), LBW (32.5%), perinatal deaths (31.3%) and nursery admission (30.6%) was more.

Limitation of this study was being retrospective as these studies are limited by their reliance on data extraction from previous records. Study is from a single center and study population mostly belonged to lower socio-economic status and may not fully representative of entire population and there were many lost to follow up cases. Finally, there was no control groups to compare outcomes.

CONCLUSIONS

Our study indicates that HIV status of the perinatal women affect the birth outcome in terms of preterm labour, low birth weight and perinatal deaths. Maximum perinatal death occurred in those cases, where women did not take any antenatal visit and presented first time in labour. Most common cause of perinatal mortality was prematurity, LBW and birth asphyxia. Overall MTCT rate of HIV was 3.4%. To conclude, overall MTCT can be prevented by timely detection, effective counseling, adequate antenatal care, ART irrespective of CD4 count and simultaneously avoiding mixed feeding.

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