Original Article

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Clinical Profile and HIV Status of the HIV Exposed Infants from Birth to 6 Months of Life

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Abstract

Background: Approximately 15-25% of HIV-infected newborns in developed countries present with a rapid disease course, with onset of AIDS and symptoms during the 1st few months of life and a median survival time of 6-9 months if untreated. In resource-poor countries, the majority of HIV-infected newborns will have this rapidly progressing disease. **Subjects and Methods:** All babies who were exposed to HIV positive mother irrespective of mode of delivery and received NVP birth dose within 6 to 12 hours of delivery and prophylaxis continued till 6 weeks according to PPTCT guidelines 2012 by National AIDS Control organization(NACO). **Results:** Among 21 babies, 19 (90.5%) babies had both parents HIV positive and in 2 (9.5%) only mother was HIV positive. Out of the 21 mothers in this study, Almost 9(42.8%) mothers had CD4 count of <350 and remaining 12(57.2%) mothers had CD4 count >350. **Conclusion:** Out of 21 babies, 15 (71.4%) were delivered by spontaneous vaginal delivery, 5 (23.8%) through LSCS and 1 (4.8%) by Instrumental (forceps) delivery.

Keywords: HIV-infected newborns, NVP birth dose, PPTCT guidelines.

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Introduction

HIV infection affects most of the immune system and disrupts its homeostasis. The pathogenesis of HIV infection and the progression to AIDS are a consequence of the properties

Of the infecting virus isolate and the host's immune response to the virus. The balance between the effectiveness of these two components determines the different outcome of the infection, from development of AIDS to long-term survival.[1]

The mucosa serves as the portal of entry for HIV, the 1st cells to be affected are the dendrite cells. These cells collect and process antigens introduced from the periphery and transport them to the lymphoid tissue. HIV does not infect the dendrite cell but binds to its DC-SIGN surface molecule, allowing the virus to survive until it reaches the lymphatic tissue.

In the lymphatic tissue (e.g., lamina propriety, lymph nodes), the virus selectively binds to cells expressing CD4 molecules on their surface, primarily helper T lymphocytes (CD4+ T cells) and cells of the monocyte-macrophage lineage. Additional factors (co-receptors) are necessary for HIV fusion and entry into cells. These factors include the chemokines CXCR4 (fusion) and CCR5. Usually, CD4+ lymphocytes migrate to the lymphatic tissue in response to viral antigens and then become activated and proliferate, making them highly susceptible to HIV infection. This antigen-driven migration and accumulation of CD4 cells within the lymphoid tissue may contribute to the generalized lymphadenopathy characteristic of the acute retroviral syndrome.[2]

HIV preferentially infects the very cells that respond to it (HIV-specific memory CD4 cells), accounting for the progressive loss of these cells and the subsequent loss of control of HIV replication. The continued destruction of memory CD4+ cells in the gastrointestinal tract leads to reduced integrity of the gastrointestinal epithelium followed by leakage of bacterial particles into the blood and increased inflammatory response, which cause further CD4+ cell loss. When HIV replication reaches a threshold (usually within 3-6 wk from the time of infection), a burst of plasma viremia occurs. This intense viremia causes flu or mononucleosis-like symptoms. With establishment of a cellular and humoral immune response within 2-4 months, the viral load in the blood declines substantially, and patients enter a phase characterized by a lack of symptoms and a return of CD4 cells to only moderately decreased level. The virus load increases by 1-4 months, and almost all HIV-infected infants have detectable HIV-1 in peripheral blood by 4 months of age.[3,4]

CD8 T cells play an important role in containing the infection. These cells produce various ligands (MIP-1α, MIP-1β, RANTES), which suppress HIV replication by blocking the binding of the virus to the co-receptors

(CCR5). HIV-specific cytotoxic T lymphocytes (CTLs) develop against both the structural (ENV, POL, GAG) and regulatory (tat) viral proteins. The CTLs appear at the end of the acute infection, as viral replication is controlled by killing HIV-infected cells before new viruses are produced and by secreting potent antiviral factors that compete with the virus for its receptors (CCR5). Neutralizing antibodies appear later in the infection and seem to help in the continued suppression of viral replication during clinical latency.[5]

A group of cytokines that includes tumor necrosis factor-α (TNF-α), TNF-β, interleukin 1 (IL-1), IL-2, IL-3, IL-6, IL-8, IL-12, IL-15, granulocyte-macrophage colony-stimulating factor, and macrophage colony-stimulating factor plays an integral role in upregulating HIV expression from a state of quiescent infection to active viral replication. Other cytokines such as interferon-γ (IFN-γ), IFN-β, and IL-13 exert a suppressive effect on HIV replication. Certain cytokines (IL-4, IL-10, IFN-γ, TGF-β) reduce or enhance viral replication depending on the infected cell type. The interactions among these cytokines influence the concentration of viral particles in the tissues. By the late stages of clinical latency, the isolated virus is phenotypically different. It grows rapidly and to high titers in culture and uses CXCR4 as its co-receptor. The switch from CCR5-receptor to CXCR4 receptor increases the capacity of the virus to replicate, to infect a broader range of target cells (CXCR4 is more widely expressed on resting and activated immune cells), and to kill T cells more rapidly and efficiently. As a result, the clinical latency phase is over and progression toward AIDS is noted. The progression of disease is related temporally to the gradual disruption of lymph node architecture and degeneration of the follicular dendritic cell network with loss of its ability to trap HIV particles. The virus is freed to recirculate, producing high levels of viremia and an increased disappearance of CD4 T cells during the later stages of disease.[6]

Approximately 15-25% of HIV-infected newborns in developed countries present with a rapid disease course, with onset of AIDS and symptoms during the 1st few months of life and a median survival time of 6-9 months if untreated. In resource-poor countries, the majority of HIV-infected newborns will have this rapidly progressing disease. It has been suggested that if intrauterine infection coincides with the period of rapid expansion of CD4 cells in the fetus, the virus could effectively infect the majority of the body's immunocompetent cells. The normal migration of these cells to the marrow, spleen, and thymus would result in efficient systemic delivery of HIV, unchecked by the immature immune system of the fetus. Thus, infection would be established before the normal ontogenic development of the immune system, causing more severe impairment of immunity.[7,8]

Subjects and Methods

Inclusion criteria:

- All babies who were exposed to HIV positive mother irrespective of mode of delivery and received NVP birth dose within 6 to 12 hours of delivery and prophylaxis continued till 6 weeks according to PPTCT guidelines 2012 by National AIDS Control organization(NACO).
- The babies should be on EBF.

Exclusion criteria:

1. Neonates who underwent any modes of resuscitation other than routine care.
2. Referred newborns without receiving NVP prophylaxis beyond >12hours of age

Methods of collection of data:

- All cases which satisfied the inclusion criteria were taken into the study.
- Purpose of the study was explained to the parents of the study subjects and informed consent was taken
- At the entry point into the study, a base line evaluation in terms of birth weight, length, head circumference and systemic examination was done.
- The following anthropometric measurements were measured as explained below.

1. Birth weight: all neonates were weighed nude on an electronic weighing scale at birth or within half an hour.
2. Length: crown heel length was recorded to the nearest of 0.5cm on a infantometer with the baby being supine, knee fully extended and sole of feet held Firmly against the foot board and head touching the fixed board.
3. Head circumference (HC) was recorded using a standard non stretchable tape as per standard guidelines.

- All these were documented in preformed proforma.
- The neonate were given birth dose of nevirapine and was advised to continue till 6 weeks.
- All mothers were counseled regarding advantages and disadvantages of both exclusive breast feeding and mixed feeding and was started on EBF on their choice.
- Babies were followed up at birth, 4weeks, 6weeks, 10weeks, 14weeks and monthly thereafter until 6 months of age and during every visit detailed history and clinical examination was performed and entered in preformed proforma.
- HIV status was evaluated at 6weeks and 6 months of life by direct blood spot for HIV -1 DNA PCR by ICTC and if it was positive it was confirmed by whole blood sample for HIV -1 DNA PCR at ART centre .
- Clinical profile and HIV status of the HIV exposed infants from birth to 6 months of life and benefits of NVP prophylaxis in infants who are on exclusive breast feeding in reducing the risk of mother to child transmission was assessed.

Statistical Analysis

Statistical analysis was done using SPSS 20 Software. Statistical methods used were percentages and means.

Results

Out of the total 50 inborn babies, 10 babies underwent resuscitation and NICU admission, 7 babies were lost for follow up and 4 babies did not receive NVP prophylaxis as advised till 6 weeks duration and hence excluded. Only 30 babies were followed up until 6 months of age, among them only 21 babies received exclusive breast feeding till 6 months of age and remaining 9 babies did not and hence the 9 babies were excluded from the study at the end of follow up period. The observations from the present study were tabulated, presented in diagrammatic form and statistical significance was derived using appropriate statistical analysis.

Table 1: Sex wise distribution of babies (n=21)

Sex	Frequency	Percent (%)
Males	13	61.9
Females	8	38.1
Total	21	100.0

Among 21 babies included in the study, 13 (61.9%) were males and 8 (38.1%) were females.

Table 2: Place wise distribution of mothers (n=21)

Place	Frequency	Percent (%)
Hubli	10	47.6
Dharwad	7	33.3
Gadag	2	9.5
Haveri	2	9.5
Total	21	100.0

Of the 21 babies enrolled, 10 (47.6%) were from Hubli, 7 (33.3%) were from Dharward, 2 (9.5%) from Gadag and 2 (9.5%) from Haveri.

Table 3: Place of delivery (n=21)

Place of delivery	Frequency	Percent (%)
Inborn	20	95.2
Out born	1	4.7
Total	21	100.0

Among the 21 babies, 20(95.2%) babies were delivered in Tertiary care and remaining 1(4.7%) baby was delivered outside and referred here.

Table 4: Occupation of fathers (n=21)

Occupation	Frequency	Percent (%)
Coolie	12	57.1
Driver	3	14.3
Farmer	2	9.5
Painter	2	9.5
Waiter	1	4.8
Carpenter	1	4.8
Total	21	100.0

Among the 21 babies in our study, the occupation of their fathers were as follows: 12 (57.1%) coolie, 3 (14.3%) driver, 2 (9.5%) farmer, 2 (9.5%) painter, 1 (4.8%) each carpenter and waiter.

Table 5: Occupation of mothers (n=21)

Occupation	Frequency	Percent (%)
Home maker	18	85.7
Farmer	1	4.8
Coolie	2	9.5
Total	30	100.0

The occupation of their mothers consisted of 18 (85.7%) home maker, 2 (9.5%) coolie, and 1 (4.8%) farmer.

Table 6: HIV status of parents (n=21)

Parents HIV status	Frequency	Percent (%)
Only mother positive	2	9.5
Both positive	19	90.5
Total	21	100.0

Among 21 babies, 19 (90.5%) babies had both parents HIV positive and in 2 (9.5%) only mother was HIV positive.

Table 7: Antenatal history (n=21)

Antenatal events	Frequency	Percent (%)
Anemia	3	14.3
Oligohydramnios	1	4.8
Gestational hypertension	2	9.5
Meconium stain amniotic fluid	2	9.5
Prolonged rupture of membrane	2	9.5
Uneventful	11	52.4

Antenatal history of mothers showed anemia in 3 (14.3%), gestational hypertension, prolonged rupture of membrane and meconium stained amniotic fluid in 2 (9.5%) each, oligohydramnios in 1 (4.8%) and it was uneventful in 11(52.4%) mothers.

Table 8: CD4 count of mothers (n=21)

CD4 count	Frequency	Percent (%)
<350	9	42.8
>350	12	57.2
Total		

Out of the 21 mothers in this study, Almost 9(42.8%) mothers had CD4 count of <350 and remaining 12(57.2%) mothers had CD4 count >350.

Table 9: Mode of delivery (n=21)

Mode of delivery	Frequency	Percent
Spontaneous delivery	15	71.4
Instrumental(forceps) delivery	1	4.8
LSCS	5	23.8
Total	21	100.0

Out of 21 babies, 15 (71.4%) were delivered by spontaneous vaginal delivery, 5 (23.8%) through LSCS and 1 (4.8%) by Instrumental (forceps) delivery.

All the 21 mothers had received some form of PMTCT measure before, during and after delivery and none of the mothers were devoid of any form of therapy or prophylaxis. Eleven mothers had received ARV prophylaxis and 10 mothers were on ART.

Table 10: Immunization status (n=21)

Immunization status	Frequency	Percent (%)
Immunized up to date	18	85.7
Not immunized up to date	3	14.3
Total	21	100.0

Of the 21 babies evaluated at the end of 6 months, 18 (85.7%) babies had received immunization up to date as per national immunization programme and 3 (14.3%) babies were not immunized up to date.

Discussion

Of the HIV exposed infants there was a male predominance over female infants (61.9% and 38.1% respectively) with M:F ratio of 1.6:1. Birth weight is generally studied because it is an established predictor of infant mortality in developed and developing countries. Perinatal mortality decreases exponentially with the increase in birth weight up to the optimum value of 3500- 3900g. A substantial increase in mortality is associated with even a modest reduction in birth weight, as in a study done in New Delhi, India, where a 22% increase in mortality could be attributed to every 10% reduction in birth weight for infants weighing ≤ 2700 g.9 In a study conducted by Kumwenda N I et al,[10] showed mean birth weight of 3.00±0.45kg in HIV exposed babies, and lower infant birth weight was associated with an increased risk of either HIV-1 infection or death.

The mean birth weight of neonates of HIV infected mothers in our study is 2.78 kg, almost same as that of standard Indian neonatal value of 2.8 kg.[11] About 14.2% of babies born to HIV positive mothers were LBW (<2.5kg) in this study as against 28% in India. Whereas 36% of babies were LBW in a study done by Gangar J.[12]

Mean birth weight noticed in our study was similar to the study conducted by Ryder et al.[13] Of the total of 21 exclusively breastfed babies, none of the babies were DNA PCR positive at the end of follow up period, at 6 months of age.

In a study conducted by Anoej C et al,[14] analysis of the DNA PCR test results showed that, regardless of infant feeding choice, the transmission rates when both mother and baby received a form of chemoprophylaxis for PMTCT was 4.8% (CI 1.3, 8.3) at zero to six weeks of age and 6.6% (CI 3.0, 10.3) at age six weeks to six months in contrast to our study which showed zero percent transmission rate both at zero to six weeks and at 6 weeks to 6 months in Exclusively breast fed infants who were on NVP prophylaxis along with appropriate chemoprophylaxis received by mother.

Infant feeding practices in the developing world that comprises almost universally of prolonged duration of breastfeeds contribute to the higher rates of 30-45 per cent of MTCT as against 15-20 per cent in the developed countries, in the absence of any intervention. The least common route of vertical transmission in industrialized nations is breastfeeding. However we observed zero percent vertical transmission risk by analyzing DNA PCR test results at 6 weeks and 6 month in exclusively breast fed infants who received birth dose plus 6 weeks of NVP prophylaxis with their mothers receiving appropriate chemoprophylaxis and PMTCT measures in the present study.

According to National guidelines for PPTCT, by NACO Women with more advanced HIV infection (CD4 < 350 cells/mm3) account for more than 75% of the HIV transmission to their child. In our study there were 9 (42.8%) mothers with CD4 count <350 but had received appropriate chemoprophylaxis as advised by PPTCT and had transmission rate of zero at end of 6 months. This may be due to the earlier initiation of ART and longer ARV prophylactic regimen for PPTCT, started earlier during pregnancy which has more benefit in preventing HIV transmission along with NVP prophylaxis received by infants up to 6 weeks and EBF up to 6 months.

Conclusion

Pediatric HIV is a huge challenge in India. Large numbers of newborns are infected with HIV each year and we can no longer ignore its magnitude. So it is very important to prevent vertical transmission of the disease from mother to child and thus the morbidity and mortality. It is important to diagnose early and treat perinatally infected infant. There is an urgent need for standardizing care of exposed infants and to promote follow-up and prevent mortality by offering feeding counseling and ensuring early detection of infections. Breast-feeding reduces diarrheal and respiratory disease morbidity and mortality among infants in the developing world, but the protection afforded by the breast milk of HIV-infected women is uncertain.

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