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Original Research Article

Study on the HIV Status of the Children Born to HIV Positive Mothers After Prophylactic Nevirapine Therapy

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Abstract:

Introduction: HIV 1 and HIV 2 are members of the Retroviridae family and belong to the lentivirus genus. HIV infection affects the immune system and disrupts its homeostasis. In 2015, WHO estimated that 1.8 million children younger than 15 yrs. of age worldwide were living with HIV 1 infection. Children contribute to one-sixth of HIV deaths and more than 95% of HIV infections in children are due to vertical transmission.

Aim: To analyze the efficacy of nevirapine prophylactic therapy in the prevention transmission of HIV infection from mother to child.

Method: This retrospective cohort study was conducted at a Pediatric Centre of Excellence in HIV Care in northern India. It focused on infants born to HIV-positive mothers enrolled in the Prevention of Mother-to-Child Transmission (PMTCT) program. This study assessed HIV status using DNA-PCR and serological tests in infants before and after national guideline changes. Maternal and infant data was obtained, including nutritional status and ethical approval.

Results: In a study involving 47 children born to HIV-positive mothers (25 male, 22 female), significant findings emerged. Of the mothers, 36% were identified as HIV-positive before pregnancy, 51% during antenatal testing, and 10% during labor. Notably, more mothers were identified during antenatal than prenatal and natal periods (P=0.047). Additionally, 6% of children tested positive for HIV after Nevirapine prophylaxis, with a significant number having negative results (P=0.041). Rural areas had more affected children (27) than urban areas (20). ELISA testing was conducted on 28% of children, revealing a 4% positive rate.

Conclusion: The implementation of Nevirapine prophylaxis therapy showed promising results, with a low proportion of HIV infection among the children born to HIV-positive mothers.

Keywords: Nevirapine, HIV, AIDS, ART, Infection.

Introduction

HIV-1 and HIV-2 are members of the Retroviridae family of viruses and are categorized as lentiviruses. Viral infections disturb immune system balance. By 2019, 1.8 million children under 15 had HIV, according to the WHO. "Antiretroviral therapy (ART)" in HIV-infected pregnant women to "prevent mother-to-child transmission (PMTCT)" reduced new infections in children aged 0-14 by 70% from 2000 to 2015 [1]. Children make up 6% of HIV-infected people but one-sixth of HIV-related mortality. "Mother-to-child transmission (MTCT)" causes 90% of HIV infections in children under 15 [1]. Infants delivered to HIV-infected pregnant mothers have a 25–45% risk of HIV infection throughout pregnancy, birth, and lactation without intervention [2]. Intrauterine (transplacental) and peripartum infections account for 25-40% and 60-75% of vertical infections when nursing is prevented. The risk of vertical transmission through breastfeeding is 8-25% in underdeveloped areas [3,4]. The "Prevention of Parent-to-Child Transmission (PPTCT)" programme and antiretroviral medication for HIV-infected children may drastically decrease HIV fatalities in this vulnerable demographic. "Mother-to-child transmission of HIV (MTCT)" occurs during pregnancy, labour, delivery, or nursing [3]. Untreated women in the US and Europe have transmission rates between 12% and 30%, but in Africa and Haiti, they are 25% to 52%. Treatment of HIV-infected pregnant women with antiretrovirals has decreased transmission to fewer than 2%. HIV transmission risk is highest during pregnancy and postpartum [4]. Half of newly infected children develop HIV during nursing. WHO infant feeding guidelines (123) emphasise the importance of ensuring that HIV-positive mothers receive "antiretroviral therapy (ART)", maintain suppressed

viral loads, and can breastfeed for up to two years, with exclusive breastfeeding for six months [5]. Breast milk transmission is low for moms on ART with decreased virus loads, and baby prophylaxis is only beneficial for the first 4–6 weeks. Breastfed babies who got "nevirapine (NVP)" for six months had a 54% reduced transmission rate than those who received just six weeks [6]. The postnatal transmission rate was very low among babies delivered to moms using ART at randomization, and there was no meaningful difference between prolonged NVP prophylaxis and a placebo. Breast milk transmission accounts for 40% of MTCT. PMTCT programmes reduced new HIV infections in children by 52% worldwide from 2001 to 2012. PMTCT depends on healthcare professionals' expertise and attitudes. HIV testing for pregnant women is followed by PMTCT counselling, HIV treatment, and thorough follow-up [7].

The WHO released revised PMTCT "antiretroviral (ARV)" recommendations in 2010, recommending Options A and B. Triple "antiretroviral treatment (ART)" for all pregnant and lactating moms, accompanied by 6-week "nevirapine (NVP)" prophylaxis for the newborn, was the most effective way to prevent HIV MTCT, according to a 2011 systematic study [8]. In 2013, WHO recommended Option B+, which provides lifelong triple-drug ART to all pregnant HIV-positive women regardless of CD4 level or clinical stage. All HIV-exposed neonates get 4-6 weeks of NVP/AZT regardless of feeding style [9]. The vertical HIV transmission risk was less than 2% with this regimen. WHO encouraged Option B+ implementation wherever possible to reduce HIV-related mortality and enhance maternal health. The "National AIDS Control Organisation (NACO)" in India began providing lifelong ART (triple medication regimen) to all pregnant and nursing HIV-positive women on January 1, 2014, following WHO recommendations from June 2013 [1,5]. This method improves maternal health and reduces the need to stop and restart ARV medicines with consecutive pregnancies, lowering vertical transmission and drug resistance. Oral nevirapine is given daily to babies for 6 weeks. The 2020 India HIV Estimation Report predicted the national prevalence of HIV among adults (15–49 years) as 0.22% (0.17%–0.29%). The national adult prevalence dropped 33.3% in the last decade. Although prevalence is low, India ranks third worldwide in HIV cases, estimated at 23.19 lakh (range 18.33 lakh–29.78 lakh) in 2020. Children under 15 had about 3.5% of infections, and 44.3% were female [10]. "National AIDS Control Organisation (NACO)" monitors HIV prevention and control policies since 1992. NACP-III reduced new HIV infections by 50%, meeting its goal of reversing the pandemic. NACP-V (2021–2026) built on NACP-IV's results to help PLHIV live longer, more productive lives [8]. The current strategic plan seeks zero new infections, zero AIDS-related deaths, and zero discrimination to abolish AIDS as a public health problem by 2030. India has one of the world's most extensive ART programmes, which provides comprehensive HIV treatment in the public health system. PLHIV have direct access to accessible diagnostic facilities, first-line therapy, second and third-line ART, PPTCT services, and a unified approach to preventing, diagnosing, and treating opportunistic infections, including daily anti-TB treatment. As a signatory to the SDGs, India aims to "End AIDS as a public health threat" by 2030 [6]. Specific 2020 Fast-Track Targets include a 75% drop in new HIV infections from the 2010 baseline, 90-90-90 treatment targets, MTCT eradication, and HIV elimination. Even with single-dose "nevirapine (NVP)" for mother-infant pairings, the research found a 6.7% vertical transfer rate in breastfeeding groups. Notably, triple ART-treated moms' newborns did not transmit HIV. This research adds to the data that triple ART is better for pregnant and nursing women than shorter regimens with fewer ARVs [11].

Materials and Methods

Research Design

This retrospective cohort study was conducted in the Pediatric Centre of Excellence in HIV Care located at a public teaching hospital in northern India. Infants born to women with HIV infection at the linked hospital and registered in the PMTCT program at our Center from January 2011 to March 2016 were included. We excluded infants born at other hospitals and subsequently referred to our centre, those diagnosed with HIV after admission to our pediatric wards, or those who never attended the centre after birth at the linked hospital.

By the National guidelines, HIV-exposed infants are registered at birth in our centre and given protocol-based care till 18 months of age [6]. This includes provision for early HIV diagnosis, safe feeding counselling, and access to routine infant care practices.

Before January 2014, all women with HIV and their newborns were given a single dose of nevirapine (SDNVP) during labor and immediately after birth, respectively, by the national guidelines at that time [7]. After January 2014, all pregnant women with HIV are initiated on ART during pregnancy soon after detection of their HIV status. Infants born to these women are started on daily nevirapine prophylaxis at birth and continued for a minimum of 6 weeks [6].

This study included subjects registered before and after these changes in the National recommendations. Determination of HIV status was done through HIV-1 DNA-PCR by dried blood spot (DBS) at ages 6 weeks, 6 months, and six weeks

after stopping breastfeeding. Infants testing positive on DBS testing were re-tested for DNA-PCR on a whole blood sample. In infants older than 18 months, serological tests (3 rapid antibody tests) were done for HIV diagnosis.

For the current study, maternal and infant characteristics information was obtained from the records of all eligible infants maintained at our centre. The nutritional status of children was determined by calculating Z-scores for weight for age (WFA), weight for length (WFL), length for age (LFA) and head circumference for age (HFA) using WHO growth reference standards [8].

The infants were considered to be HIV-infected if they tested positive on DNA-PCR any time before 18 months or were found reactive on HIV serology at 18 months or beyond. They were considered HIV-uninfected if they had a negative DNA-PCR test and were not breastfeeding or had stopped it 6 weeks before the test, or had a non-reactive HIV serological test at or after 18 months performed at least 6 weeks after cessation of breastfeeding. The Institutional Ethics Committee approved the study for Human Research.

Statistical Analysis

The data were analyzed using the SPSS statistical software package, Version 23. The chi-square test, unpaired t-test and Mann-Whitney U test were used to compare maternal and infant variables among HIV- uninfected infants at 18 months and those who died.

Result

In our study, we enrolled 47 children born to HIV-positive mothers, out of which 25 were male and 22 were female.

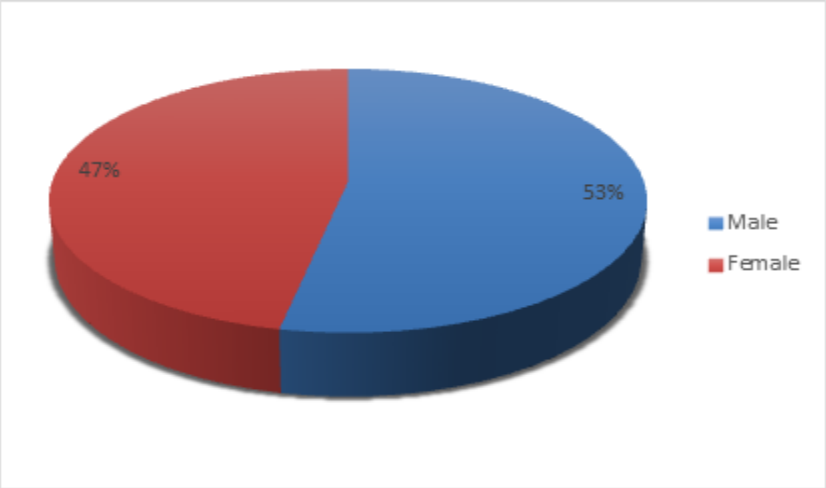

Figure 1: Distribution of gender in this study

Out of 47 women included in the study, 17 (36%) mothers were identified as HIV infected before pregnancy, 24 (51%) during antenatal testing and 5 (10%) during labour. The study has shown that there is significant number of mothers identified as HIV positive during antenatal period as compared to pre-natal and natal period (P=0.047).

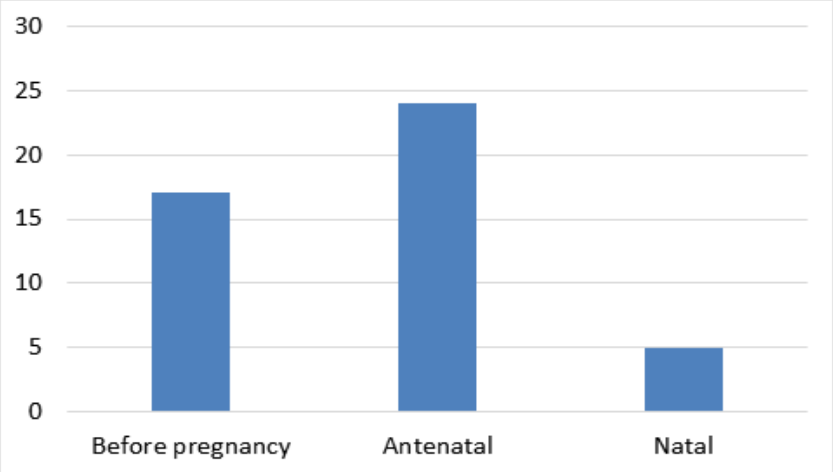

Figure 2: Number of mothers identified as HIV positive at each stage

6 weeks of DBS were done in all children born to HIV-positive mothers except 1 (lost to follow-up), out of which 3 (6%) came out to be positive 43 (91%) were negative and all received Nevirapine prophylaxis. It was found that significant number of children had negative HIV (P=0.041).

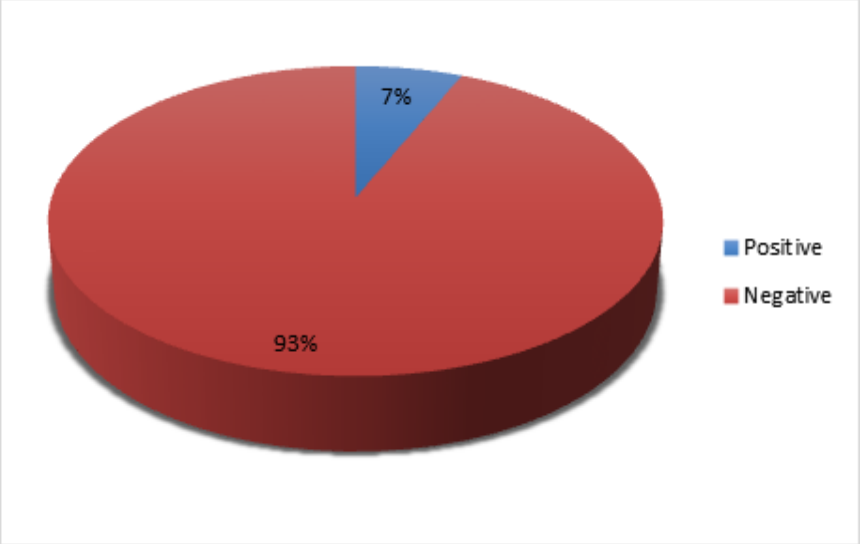

Figure 2: Proportion of HIV infection among the children of HIV-positive mothers after Nevirapine prophylaxis therapy

The children of those HIV-positive mothers were more from rural areas (27 children) as compared to the urban areas (20 children).

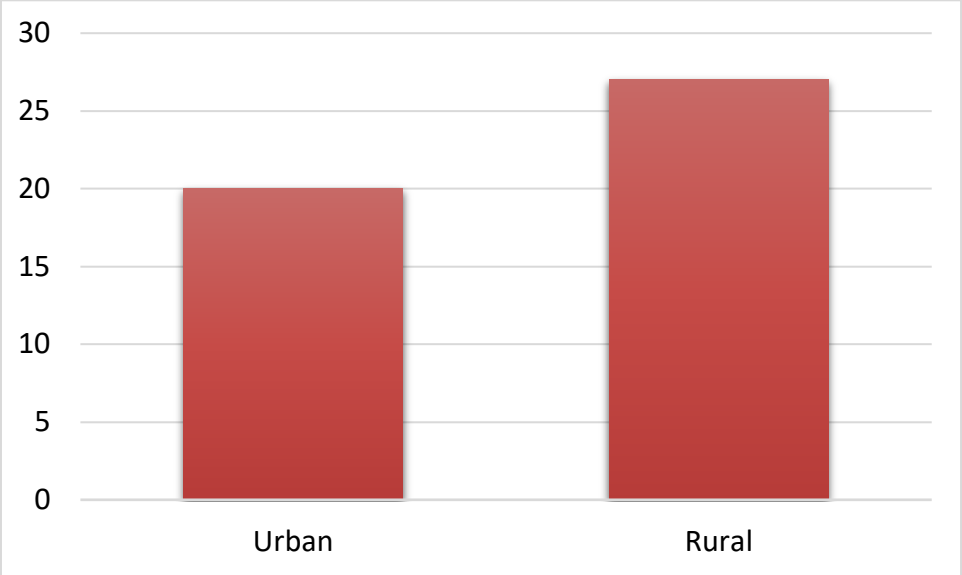

Figure 3: Proportion of HIV infection among the children of HIV-positive mothers after Nevirapine prophylaxis therapy

ELISA test is done on only 13 (28%) children out of the total children included in the study, as 34 (72%) of children are <18 months of age. Of the total number of children tested for ELISA, 2 (4%) came out positive.

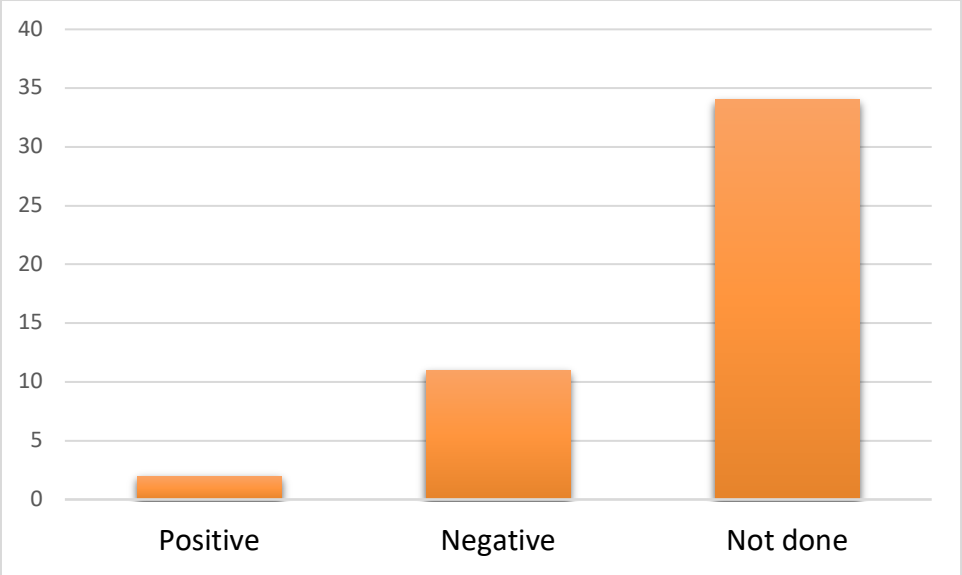

Figure 4: ELISA results at 18 months

Discussion

The "National AIDS Control Organisation (NACO)" pilot research predicted 10–20% parent-to-child transmission, whereas this study found 4% [1]. It matches Chennai research that found 8.3% transmission from 218 dried blood spot DNA PCR samples [5], while other investigations have shown greater transmission rates [6,7]. Marinda et al. [8] found that HIV-positive women with severe illnesses were more likely to infect their babies. In contrast to predictions, all four PCR-positive infants were delivered to stage 1 or stage 2 women with CD4 counts over 350 cells/mm3. In contrast, Marazzi et al. [9] found a 50.6% transmission rate from non-ART-using moms with CD4 levels over 350 cells/mm3. Ugochukwu et al. [10] found that triple-drug ART reduced transmission even in advanced maternal illness or low CD4 levels. Since single-dose Nevirapine may cause resistance [14,15], recent recommendations and numerous studies recommend triple-drug regimens to prevent parent-to-child HIV transmission [11-13]. The transmission rates were 6.7% and 0% in breastfed and non-breastfed groups, respectively, although three of the four babies were PCR-positive at 6 weeks of life [16-19], suggesting intrapartum transmission. Using non-breastfeeding methods, Palombi et al. [15] showed a transfer rate of less than 2% and no increase in mortality. Our research agrees with an earlier one [9] in that the cumulative HIV-free survival at 18 months is similar.

A limited sample size and a study population mainly from the poor and lower-middle class may restrict the generalizability of our results. However, we conclude that when pregnant women get "antiretroviral treatment (ART)", newborns are given a single dose of Nevirapine, and mixed feeding is avoided [20-23], the risk of HIV transmission from parent to child is significantly reduced. "Mother-to-child transmission (MTCT)" is the most common route of HIV infection in children less than 14 years old, and it may occur during pregnancy, delivery, and nursing. With ART and other therapies, the probability of viral transfer from mother to kid may be lowered to below 5% from 15% to 45%. The implementation of PMTCT services has been critical, averting an estimated 1.4 million new paediatric HIV infections between 2010 and 2018 [24].

Breastfeeding infected half of the 180,000 HIV-positive infants in 2017. They were maintaining HIV-positive women in care and on effective ART while breastfeeding is difficult. This involves preventing, detecting, and treating pregnant and nursing infections. Therefore, postnatal newborn illnesses are now more common in certain countries than pregnancy or labour [25]. All parents in our research got breastfeeding information and counselling on its pros and cons. The majority (85%) chose the formula. They received extra training in formula milk preparation and feeding with a spoon and bowl, following all sanitary guidelines. HIV-positive nursing mothers with viral load data are understudied. The research implies that undetectable viral loads protect against HIV transmission. HIV has been transmitted to nursing mothers with undetectable viral loads [26].

The need for PMTCT programmes to prioritise ART compliance during breastfeeding is growing. Women sometimes progressively stop taking ARV medicines after delivery, endangering their health and increasing the risk of HIV transmission to their babies during nursing. A significant assessment of Kenya, South Africa, the USA, and Zambia found that 76% of pregnant women used ART during pregnancy, but only 53% did so after having

children [27]. South African research found that incorporating postnatal HIV therapy into maternal, neonatal, and child health care greatly improved results. 77% of moms receiving ART via integrated services had viral suppression, compared to 56% of those receiving separate therapy [28]. Our research found no gender difference in HIV-positive moms' children. In February 2005, Taha et al. in Malawi, South Africa, found that female newborns may be more vulnerable to HIV before and after delivery. Alternatively, the greater in-utero death rates of HIV-infected male newborns may lead to more HIV-infected female infants [29].

Everyone in the trial got Nevirapine prophylaxis, which significantly reduced HIV incidence in HIV-positive mothers' children. Bhatta et al.'s September 2020 meta-analysis found that children who did not get ARV prophylaxis at or after birth were more vulnerable to HIV infection than those who did. ARV pre- and post-exposure prophylaxis protects neonates against HIV transmission [30]. Most of the women in the study who were HIV positive gave birth in medical settings where they received standard medical care and adequate PMTCT measures. Women with HIV infection who did not get adequate medical care during childbirth were more likely to have HIV-positive offspring than women with HIV infection who got treatment from competent medical technicians in healthcare facilities [31]. This was the finding of another research by Bhatta et al. [30].

Conclusion

In conclusion, our study focused on the HIV transmission rates among children born to HIV-positive mothers and the effectiveness of Nevirapine prophylaxis therapy. The findings revealed that a significant number of mothers were identified as HIV positive during the antenatal period compared to the prenatal and natal periods. This emphasizes the importance of early detection and intervention during pregnancy to minimize the risk of mother-to-child transmission. The implementation of Nevirapine prophylaxis therapy showed promising results, with a low proportion of HIV infection among the children born to HIV-positive mothers. This highlights the effectiveness of this preventive measure in reducing the transmission of the virus from mother to child.

Moreover, our study observed a higher prevalence of children from rural areas compared to urban areas among HIV-positive mothers. This distinction underscores the need for targeted interventions and healthcare access in rural settings to address the unique challenges faced by this population. It is worth noting that the ELISA test, performed on a subset of children due to their age, revealed a relatively low rate of positive results. This underscores the success of early interventions and the importance of ongoing monitoring and testing to ensure the sustained health of children born to HIV-positive mothers. In summary, our study contributes valuable insights into the dynamics of mother-to-child HIV transmission, emphasizing the significance of early detection, Nevirapine prophylaxis therapy, and tailored interventions for different geographic settings. Further research and ongoing monitoring are essential to continually improve strategies for preventing and managing HIV transmission in this vulnerable population.

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