

Evaluation of infants with HIV-infected mothers and perinatal transmission in Turkey: A single-center experience

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ABSTRACT

OBJECTIVE: The most common route of HIV infection in children is through perinatal transmission. In this study, we aimed to evaluate the characteristics of infants with HIV-infected mothers and perinatal HIV transmission.

METHODS: We conducted a retrospective, single-center study of HIV-exposed infants in between December 2017 and October 2019 in a Marmara University Pendik Training and Research Hospital.

RESULTS: A total of 18 infants were examined. All babies were born by cesarean section, and none of them were breastfed. Seventeen mothers were diagnosed with HIV before pregnancy. These mothers had received antiretroviral therapy (ART) during pregnancy, and their viral loads before delivery were negative. An antiretroviral prophylaxis with oral zidovudine was started in all infants within their 1st day of birth and continued for at least 6 weeks. All infants were tested for their HIV viral load within the first 48 h of birth, with negative results, and 12 infants were tested for anti-HIV antibodies at the 18th month, again with negative results. In this study, we determined that none of the infants had been infected with HIV.

CONCLUSION: Our findings highlight the importance of initiating ART for all HIV-infected pregnant women and the importance of protection modalities during pregnancy, delivery, and the postnatal period for the prevention of perinatal transmission of HIV.

Keywords: Children; HIV; infection; perinatal transmission; Turkey.

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According to data from the Joint United Nations Program on HIV/AIDS (UNAIDS), 36.7 million people worldwide are infected with HIV and 1.8 million are newly diagnosed [1]. The first AIDS case was reported in Turkey in 1985. The Turkish Ministry of Health reports that in Turkey, there are 21,988 patients with a diagnosis of HIV or AIDS and that 718 of these people are children or adolescents [2]. Perinatal transmission, also known as vertical or mother-to-child transmission, is the main route of HIV infection in children. It is estimated that there are 2 million

children living with HIV infection worldwide [3]. Pediatric HIV infection can occur during pregnancy, delivery, or breastfeeding. The rate of transmission without intervention ranges from 15% to 35% [4, 5]. However, perinatal transmission of HIV can be prevented by taking precautions in the perinatal period, and the probability of transmission can be reduced to below 2% with plasma HIV viral load suppression [6, 7]. Prevention of perinatal transmission of HIV is possible using the following measures: Antiretroviral therapy (ART) throughout the pregnancy, cesarean

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section birth at the 39th week, administration of an antiretroviral prophylaxis to the newborn, physician care, and elimination of breastfeeding. This study aimed to evaluate the characteristics of infants with HIV-infected mothers and perinatal transmission at a tertiary care hospital in Turkey.

MATERIALS AND METHODS

Study Design and Data Collection

This retrospective single-center study examined 18 infants with HIV-infected mothers at a pediatric infectious disease outpatient clinic in a tertiary care hospital in Turkey. The medical records were collected from patients who attended our hospital between December 2017 and October 2019. The following demographic and laboratory data were collected retrospectively: Gender; birth weight; gestational age; type of delivery; obstetric history (gravida or parity); maternal follow-up period and ART regimen; antiretroviral (ARV) prophylaxis; laboratory results including leukocyte, lymphocyte, platelet counts, and hemoglobin level within 48 h and after administration of the ARV prophylaxis; HIV RNA levels within the first 48 h, at postnatal 2nd week, 4th week, 4th month, and 6th month; and the presence of HIV antibodies at the 12th month and the 18th month.

Statistical Analysis

Data were entered into Microsoft Office Excel 2010 (Microsoft; Redmond, WA, USA). The statistical analysis was performed using SPSS version 21.0 (SPSS Inc.; Chicago, IL, USA). Mean, median, minimum, and maximum values were used for continuous variables. Frequencies and percentages were used to summarize categorical data.

Ethical Approval

The Clinical Research Ethics Committee of Marmara University Faculty of Medicine approved this study (Date: 04.09.2020 and Decision no: 09.2020.945).

RESULTS

A total of 18 infants and their HIV-infected mothers were examined during the study period. There were 7 (39%) female and 11 (61%) male infants. The median and mean birth weight were 3045 g and 3011.39±674.726 (range 1700–4320) g, respectively. None of the infants

Highlight key points

- HIV perinatal transmission is an important cause of children mortality worldwide. In this study, none of the infants haven't become infected with HIV.
- The number of cases with HIV infection is increasing in Turkey.
- There are a little data about HIV exposed infants and perinatal transmission in Turkey.
- Antiretroviral therapy for mothers and prevention modalities is important to reduce, even eliminate perinatal HIV transmission.

breastfed. There were two preterm, and two low birth weight infants in our study sample. All infants were given ARV prophylaxis with oral zidovudine (ZDV) for at least 6 weeks. The dosage of ZDV was determined according to gestational age. ZDV was started 4 mg/kg twice daily except two preterm infants. The demographic characteristics of the infants and mothers are summarized in Table 1. Seventeen mothers had been diagnosed with HIV before pregnancy and received ART during pregnancy. One mother delivered at the another center has received intrapartum prophylaxis with intravenous (IV) ZDV. The ART regimen of mothers is shown in Table 2.

HIV RNA analysis for the infants was performed within the first 48 h of birth, at postnatal 2nd week, 4th week, 4th month, and 6th month. There were 18 infants available for testing within the first 48 h, 14 infants at the postnatal 2nd week, 15 infants at the 4th week, 17 infants at the 4th month, and 15 infants at the 6th month. All results came back negative. Anti-HIV analysis was performed at the 12th month and the 18th month. There were 12 infants tested for anti-HIV antibodies at the 18th month with all results found to be negative. HIV RNA analysis before delivery produced negative results in 17 mothers who received ART during pregnancy. The mean white blood cell (WBC) and lymphocyte counts within the first 48 h were 12911.11±3059.39 (range, 8200–20300)/mm³ and 6038.89±1891.19 (range, 2800–10200)/mm³, respectively. The mean WBC and lymphocyte counts at the 6th week were 10433.33±2758.51 (range, 5700–16000)/mm³ and 6700±2574.99 (range, 2500–12000)/mm³, respectively. The laboratory findings of the infants are summarized in Table 3. No adverse effects related to ZDV were observed in any of the infants. All infants tested negative for HIV at their last follow-up.

TABLE 1. The demographic characteristics of the infants and mothers

| Variable | n | % |
|--|-----------|------------------------|
| Gender | | |
| Female | 7 | 39 |
| Male | 11 | 61 |
| Hospital of birth | | |
| Our hospital | 10 | 55 |
| Other hospital | 8 | 45 |
| Type of delivery | | |
| Spontaneous vaginal deliver | 0 | 0 |
| Cesarean delivery | 18 | 100 |
| Breastfeeding | | |
| No | 18 | 100 |
| Yes | 0 | 0 |
| Antiretroviral prophylaxis | | |
| No | 0 | 0 |
| Yes | 18 | 100 |
| Ethnicity of mother | | |
| Turkish | 15 | 83 |
| Other | 3 | 17 |
| HIV status at last follow-up | | |
| Not infected | 18 | 100 |
| Infected | 0 | 0 |
| | Min–Max | Mean±SD |
| Admission age (days) _(median) | 1–75 | 65±72.56 (34) |
| Last follow-up age (months) _(median) | 7–54 | 25.39±13.695 (23) |
| Duration of babies follow-up (months) _(median) | 6–48 | 23.2±12.2 (20.5) |
| Birth weight (g) _(median) | 1700–4320 | 3011.39±674.726 (3045) |
| Gestational age at birth (week) _(median) | 32–40 | 37.5±2.176 (38) |
| Duration of mother’s ARV treatment (years) _(median) | 0.5–10 | 4.083±2.7667 (4) |

HIV: Human immunodeficiency virus; ARV: Antiretroviral; Min: Minimum; Max: Maximum; SD: Standard deviation.

DISCUSSION

Although the number of new HIV infections, as well as perinatal infections, has fallen in the United States, perinatal transmission is one of the most important challenges facing developing countries in the HIV epidemic [8, 9]. The majority of children with HIV have acquired it through perinatal transmission, during pregnancy, at childbirth, or from breastfeeding [10]. Therefore, the prevention modalities of ART during pregnancy and delivery, cesarean delivery, and postnatal ARV prophylaxis for the infant are the keys to reducing new HIV infection in children [11, 12]. In Turkey,

TABLE 2. Antiretroviral therapy regimen of mothers

| Drugs | % |
|---|------|
| Emtricitabine/tenofovir+raltegravir | 41 |
| Emtricitabine/tenofovir+lopinavir/ritonavir | 35 |
| Elvitegravir/cobicistat/emtricitabine/tenofovir | 23.5 |
| Zidovudine/lamivudine+lopinavir/ritonavir | 0.5 |

limited studies have evaluated the perinatal transmission of HIV and infection outcomes [13, 14]. In this

TABLE 3. The laboratory findings of the infants with HIV-infected mothers

| Variables | Min-Max | Mean±SD |
|---|-----------------|-----------------------|
| Hemoglobin [in the first 48 h, g/dl (median)] | 10.4–19.3 | 14.48±1.74 |
| WBC [in the first 48 h,/mm ³ (median)] | 8200–20.300 | 12911.11±3059.39 |
| Thrombocytes [in the first 48 h/mm (median)] | 16.000–496.000 | 302,611.11±71,229.65 |
| Lymphocytes [in the first 48 h/mm ³ (median)] | 2800–10.200 | 6038.89±1891.19 |
| Hemoglobin [at the 6 th week, g/dl (median)] | 8.2–13.4 | 11.01±1.50 |
| WBC [at the 6 th week,/mm ³ (median)] | 5700–16.000 | 10433.33±2758.51 |
| Thrombocytes [at the 6 th week, /mm (median)] | 210.000–583.000 | 445,944.44±116,695.44 |
| Lymphocytes [at the 6 th week, /mm ³ (median)] | 2500–12.000 | 6700±2574.99 |
| Granulocytes [at the 6 th week, /mm ³ (median)] | 1700–3600 | 2244.4±835.40 |

SD: Standard deviation; Min: Minimum; Max: Maximum; WBC: White blood cell.

study, we examined the characteristics of infants with HIV-infected mothers and perinatal transmission at a tertiary care hospital in Turkey.

As reported by the Turkish Ministry of Health in 2019, the rate of perinatal transmission was 0.47% (n=18) from January 2018 to December 2018 [2]. A study by Gülümser and Erbaydar investigated epidemiologic characteristics for HIV/AIDS in Turkey between 1985 and 2013 and reported that the rate of perinatal transmission has increased proportionally over time with 0.37% increase in the past 2-year period [15]. In two studies conducted in our country, Sutcu et al. [13] and Inkaya et al. [14] demonstrated that the rate of perinatal transmission was 6.2% and 8.3%, respectively. In this study, we did not observe any cases of perinatal transmission over the period of the study. Worldwide, developing countries with a high prevalence of HIV infection have developed policies, prevention modalities, and created follow-up organizations to reduce the incidence of perinatal transmission. Despite the efficacious interventions and the significant reduction of perinatal transmission of HIV in many of these countries, it continues to be a problem. In contrast, studies conducted in developed countries report a low perinatal transmission rate of 1.2–1.4% [16–18]. Furthermore, the rate of transmission is increasing in developing countries. In large cohort studies with HIV-exposed infants, the rate of perinatal transmission was reported to be 7.8% by Potty et al., 8.2% by Okoko et al., 5.9% by Read et al., and 8.9% by Mints-Ndong et al. [19–22]. One of the most important interventions for avoiding perinatal transmission of HIV is ART for all HIV-positive preg-

nant women [23]. Many previous studies have shown that ART is effective in reducing the risk of perinatal transmission of HIV [24–27]. A cross-sectional survey study of HIV-exposed infants demonstrated that ART used during their mothers' pregnancy was associated with a low perinatal transmission rate of 1.58% [26]. In the present study, almost all the mothers (94.5%) received ART during pregnancy. In addition, all infants in our study sample were given an ARV prophylaxis with oral ZDV for at least 6 weeks following birth as giving an ARV prophylaxis to the newborn immediately after birth reduces the risk of perinatal HIV transmission. The protection afforded by the prophylaxis against the virus is due to its access to the infant's bloodstream and the unintegrated virus that helps to prevent perinatal transmission [28, 29]. In a cross-sectional study conducted on HIV-exposed infants, Yitayew et al. [30] reported that ARV drugs given to the mother during pregnancy and the administration of an ARV prophylaxis to the infant was the two most significant factors in avoiding perinatal HIV transmission. In a systematic review, Lumaca et al. [31] reported that an optimal ART regimen and the use of intrapartum ZDV for pregnant women are recommended to reduce perinatal HIV transmission. One mother in this study who gave birth at another hospital received an intrapartum prophylaxis with IV ZDV.

The other important preventive methods against perinatal HIV transmission are elective cesarean section and not breastfeeding if safety formula feeding can be accessed [32]. In this study, all infants were born by cesarean section, and none of them were breastfed.

The important limitations of this study were its retrospective, single-center design, and small sample size.

Conclusion

It is possible to reduce, even eliminate, perinatal HIV transmission with preventive modalities. In this study, we determined that none of the infants in the study became infected with HIV during the study period. Our results reaffirm the benefits of ART for mothers, ARV prophylaxis for infants, birth by cesarean section, and avoidance of breastfeeding. Further multicenter studies with a larger number of patients are needed to provide more reliable results.

Ethics Committee Approval: The Marmara University Clinical Research Ethics Committee granted approval for this study (date: 04.09.2020, number: 09.2020.945).

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