

# Twenty Years of Improved Perinatal Outcomes for Pregnancies Affected by HIV Infection

## Abstract

**Background:** Highly active antiretroviral therapy has emerged as an essential treatment component to prevent vertical transmission of Human Immunodeficiency Virus (HIV). Yet there often remain missed opportunities to prevent vertical HIV transmission. We present a case that illustrates obstetric management and outcome for involving 2 generations of congenital HIV transmission.

**Presentation of the Case:** Patient is a 19-year-old primigravida with congenital HIV presented to Lincoln Medical and Mental Health Center's for her initial prenatal care at 36 weeks of gestation. Upon documentation of a high viral load, the patient was given intravenous Azidothymidine and scheduled for Caesarean delivery. AZT and lamivudine were recommended and prescribed for the neonate who tested positive HIV test for which AZT and lamivudine were recommended and prescribed, but the mother discontinued AZT after discharge from the hospital. At 1 month of age the infant succumbed to sudden infant death syndrome (SIDS). During the 2nd pregnancy the patient received adequate prenatal care as well as antiretroviral therapy, Truvada, Abacavir, Mepron, and Kaletra throughout the antenatal course. After preoperative intravenous AZT, via a repeat cesarean the patient delivered a neonate whose HIV test was negative. The patient's 2nd child had an uncomplicated neonatal course and was negative for HIV on 3 subsequent tests and remained HIV negative until this date. Antiretroviral were removed and the child has remained HIV negative. The mother died from pneumonia and respiratory failure secondary to HIV 2 years after the 2nd delivery.

**Conclusion:** This case serves as a reminder of the importance of adhering to current clinical standards for the care of pregnancies affected by HIV infection.

**Keywords:** Acquired Immune Deficiency Syndrome (AIDS) ; Azidothymidine (AZT); AZT resistance; Highly Active Antiretroviral Therapy (HAART); HIV Viral Load (VL); Human Immunodeficiency Virus (HIV); Human Immunodeficiency Virus and Acquired Immune Deficiency Syndrome (HIV/AIDS); Mother-To-Child Transmission (MTCT); Vertical Transmission; Zidovudine (ZDV)

## Introduction

Since the 1990's highly active antiretroviral therapy (HAART) been established as a way to increase perinatal survival in symptomatic HIV patients with CD4+ count <500 cells per cubic millimeter [1-3]. Subsequent investigators have demonstrated that improved outcomes can be realized with the use of HAART in asymptomatic HIV patients [4].

According to the 2012 UNAIDS report, worldwide in 2013 an estimated 240,000 infants and children were newly infected with HIV via vertical transmission, with 90% of those infections occurring via maternal to child transmission. According to the Centers for Disease Control and Prevention (CDC) at the end of 2012, the estimated number of people living with Human Immunodeficiency Virus (HIV) in the United States and dependent areas was 914,826 [5]. This included 2,548 children under age of 13 and an estimated number of US children infected annually via perinatal transmission of HIV of 150 [6].

Careful measures have been established to prevent perinatal transmission of HIV, such as monitoring viral load during pregnancy to assess risk of perinatal transmission [7]. In order to prevent perinatal HIV transmission due to rupture of membranes, scheduling caesarean delivery at 39 weeks has been established as a means to reduce perinatal transmission of HIV [8]. The importance of administration of intrapartum Zidovudine has also been demonstrated [9,10]. While improvements have been made in survival of HIV infected children using HAART [11], many of these cases are preventable. We present a case of three generations of perinatal transmission of HIV. In describing the case we demonstrate the consequences of late versus early intervention in the outcomes of the children.

## Presentation of the Case

Patient is a 19 year old, Hispanic female acquired congenital HIV at time of birth. When patient was at 5 years of age; both of her parents died from AIDS. Her brother died at age of 15 from congenital AIDS. The patient was raised by her maternal

## Case Report

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grandmother. The patient presented to prenatal clinic at 36 weeks of pregnancy for her initial prenatal care. Despite being on Highly Active Antiretroviral Therapy (HAART), Diflucan and Zithromax, viral load was still 21,000 copies/mL, CD 4+ count was 132 cells/mm<sup>3</sup>. Therefore, patient was scheduled for primary cesarean section at 38 weeks as per protocol.

### First pregnancy

In November 2006, patient was given intravenous AZT prior to elective primary cesarean delivery at 38 2/7 wks due to HIV high viral load 21,200 copies/ml and with a CD 4 count of 132 cells/mm<sup>3</sup> (on October 2006). A male live infant was delivered via cesarean with APGAR of 9 at 1<sup>st</sup> minute and 9 at 5<sup>th</sup> minute. Neonatal weight was 3145 grams. Baby was transferred to Neonatal Intensive Care Unit (NICU), for antiretroviral therapy and management of transient tachypnea and pneumonia.

On postoperative day 3, patient was transferred to Medical Intensive Care Unit (MICU), for community acquired pneumonia due to acute exacerbation of cystic bronchiectatic lungs that was associated with *Pseudomonas Aeruginosa*. Clinical improvement occurred after Zosyn/Tobramycin treatment was started. The patient and her baby were discharged on postoperative day #10.

The infant tested positive on HIV-1 screening test and was treated and discharged on Azidothymidine (AZT) and Lamivudine. The mother discontinued azidothymidine when the child was one month of age. At 2 months of age on February 2007, the infant was brought to the emergency department with death on arrival (DOA) due to Sudden Infant Death Syndrome (SIDS), as the cause of death. The infant had 3 visits to the pediatric clinic. Infant had appropriate number of visits to pediatrician, as baby was still hospitalized for 1<sup>st</sup> week visit and usual scheduled visit is on 1 week, 2 week, one month and 2 months follow up.

Per review patient's chart, patient was supposed to get Depo-Provera as form of birth control, which later she changed her mind to use of condom for future contraception.

### Second pregnancy

In September 2007, patient treated with Truvada, Abacavir, Mepron and Kaletra became pregnant by a different partner. Her HIV viral load was 20,400 copies/mL with a CD 4 count of 148 cells/mm<sup>3</sup>. Following preoperative intravenous Azidothymidine (AZT), Patient underwent a repeat cesarean at 39 6/7 weeks on May 2007 due to HIV high viral load of 66,800 copies/ml on March 2007. Neonatal weight was 3,680 grams with APGAR was 9 at 1<sup>st</sup> minute and 9 at 5<sup>th</sup> minute. Postoperative course was complicated by for acute respiratory failure secondary to bilateral pneumonia and exacerbation of bronchiectasis. The patient was transferred to medical intensive care unit (MICU) and was discharge home on Day 9.

The patient's second neonate was immediately treated with antiretroviral therapy and had an uneventful peripartum course. After 3-polymerase chain reaction (PCR) test for HIV were negative, the second child's antiretroviral therapy was discontinued. The child has remained well with negative HIV tests up to last visit.

### Third pregnancy

In December 2008, while patient was on HAART, with a HIV viral load was 39,700 copies/mL (on September 2008) and reported CD count of 151 cells/mm<sup>3</sup> on 9/2008, massive ascites was noted at 16+ weeks of gestation. Patient underwent abdominal paracentesis twice. Elective termination of pregnancy was performed. The patient was received the diagnosis of Non-Hodgkin's lymphoma (NHL) - large cell lymphoma stage IV was diagnosed. Patient expired from sepsis secondary to pneumonia and respiratory failure in February 2009 at age 21. The patient's second child receives health care at our institution and continues to have negative HIV tests.

### Discussion

The case we present supports the timely and ongoing prenatal administration of antiretroviral agents. Despite eventual overwhelming infection in the mother, vertical transmission during the 2<sup>nd</sup> pregnancy vertical transmission was likely prevented by the administration of antiretroviral therapy before and during pregnancy. Recent work by the INSIGHT START Study Group has demonstrated antenatal HAART therapy was associated with increased survival in early asymptomatic HIV patients with CD4+ count >500 cells per cubic millimeter [4]. Initiating early HAART in asymptomatic HIV positive women of childbearing age could serve as an effective means of preventing perinatal transmission combined with careful prenatal care.

Other studies echo our case advocating for early HAART in pregnancy, showing reduction of perinatal HIV transmission to 25-28 % [12]. More recent work has demonstrated that HAART before conception drastically decreased transmission. In a French study by Mandelbrot et al. [13] maternal to child transmission was 0.7% (56/8075) in mothers who received HAART [13]. It is important to note that in this study, patients were on at least 3 antiretroviral prior to conception; our patient was only on Zithromax supplemented with Diflucan prior to her first pregnancy. Using the combination of 4 drugs described, along with intrapartum AZT, perinatal transmission of HIV there was no vertical transmission of HIV during the second pregnancy. While antiretroviral therapy can be started at any time during the pregnancy, treatment delays during the prenatal period has been shown to the risk of vertical transmission [14,15].

The importance of lowering the risk of HIV transmission via breastfeeding has been well established [16]. Although it is recommended for HIV positive women who chose to breastfeed be provided with HAART, in developed countries there have still been reported cases of HIV transmitted during breastfeeding [17]. Additionally, the toxicity of antiretroviral drugs to the infant via breast milk has not been fully established due to varying drug concentrations in breast milk between drugs [18].

Despite the advances made in our understanding of HIV transmission, opportunities are missed in preventing transmission, as is demonstrated in our case. A study in Georgia (USA) found that in 27 cases of Mother-To-Child Transmission (MTCT), 52% did not receive HAART during pregnancy or intrapartum AZT [19]. Barriers to adequate antiretroviral therapy before and during pregnancy include patient adherence, literacy, formal

education and knowledge of HIV [20,21]. Early identification of these social-economic factors may serve as an important tool to assist in efforts to prevent perinatal transmission of HIV. In addition, to facilitate early identification of vertical transmission, it is important to repeat HIV testing in the third trimester during labor in areas of high HIV prevalence [22].

## Conclusion

While great advances have been made in our understanding of Mother-To-Child Transmission (MTCT) of HIV, preventable transmission still occurs. Due to the continuing increase in the rise of HIV among reproductive adults, it is important to maintain increased clinician awareness of treatment guidelines for HIV in pregnancy. Our case of 2 congenital generations of HIV transmission highlights the perinatal outcomes associated with prenatal HAART. Incredible scientific advances have been made in the prevention of HIV transmission. Even though the clinical relevance of HIV infection has primarily become as a chronic disease, health care providers should remain adherent to best practice guidelines as a means to prevent perinatal HIV transmission.

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