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ORIGINAL ARTICLE

Epidemiological description of children vertically exposed to HIV in a tertiary pediatric hospital in Santa Catarina

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Abstract

Introduction: Acquired immunodeficiency syndrome was first recognized in the United States in 1981, with global spread in the last four decades. Although the number of new infections in children is decreasing, it still remains unacceptably high, causing severe immunosuppression if treatment is not carried out in a timely manner. **Objectives:** to describe the epidemiological profile of pediatric patients vertically exposed to HIV treated at a tertiary referral hospital in Santa Catarina. **Method:** an epidemiological, observational, analytical, cross-sectional study with retrospective data collection from January 2015 to December 2020 by CID Z 206 (contact with and exposure to the human immunodeficiency virus - HIV). The research was approved by the Ethics and Research Committee on Human Beings (CEP) of the institution. **Results:** There were 678 medical records analyzed, with 579 (85.4%) white, 348 (51.0%) males, mean age of 324 days and maternal diagnosis of HIV prior to pregnancy in 434 (64.0%) cases. Most of these, 601 (88.6%), used antiretroviral therapy. Viral RNA (viral load) in 414 (61.0%) pregnant women was undetectable and 376 (55.4%) underwent intravenous zidovudine at delivery. The first viral load of those exposed was undetectable in 606 (89.3%) patients and 667 (98.3%) were not breastfed. Fourteen patients (2%) confirmed HIV infection, and all started antiretroviral therapy. **Conclusion:** Most pregnant women living with HIV had adequate prenatal care, however, with a high prevalence of syphilis. The rate of HIV-positive newborns was equivalent to the literature, but with incomplete prenatal care.

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INTRODUCTION

The first cases of acquired immunodeficiency syndrome (AIDS) were reported in 1977. In Brazil, the first case was diagnosed in 1980. In 1983, the first pediatric case of the disease was described. Treatment with zidovudine (AZT) was initiated in 1987[1].

The human immunodeficiency virus (HIV) is a retrovirus with a ribonucleic acid (RNA) genome that uses the enzyme reverse transcriptase to replicate[2]. HIV attacks the immune system, especially CD4+ T lymphocytes, and can cause AIDS, which makes patients vulnerable to opportunistic diseases, including infection and some types of cancer[1].

The AIDS detection rate in children under five years of age is used as an indicator of vertical transmission of the virus, which has decreased by 47.2% in Brazil over the last ten years. Such decrease has been universally observed in all country regions, with sharper drops occurring in the South[3]. According to data from the Joint United Nations Programme on HIV/AIDS (UNAIDS, 2021), 79.3 million people have been infected since the beginning of the pandemic, and 36.3 million have died from diseases related to the infection. In 2020, there were 37.7 million people with HIV worldwide – 36 million adults plus 1.7 million children under the age of 15. An estimated 35 million people living with HIV are unaware of their serological status[1]. According to the Brazilian HIV/AIDS epidemiological report (2020), a total of 1,011,617 cases of AIDS were reported from 1980 to June 2020, with an average annual 39,000 new cases in the last five years. The number of cases has been decreasing since 2013[3].

Worldwide, 1.6 million new infections in children were prevented between 2008 and 2017 due to the increase in the number of women living with HIV receiving antiretroviral therapy (ART) to prevent vertical transmission. However, efforts are hampered by poor adherence to treatment among pregnant and lactating women living with HIV and by a lack of knowledge of their serological status for the virus[1].

Treating pregnant women with ART has caused a 20-fold decrease in HIV transmission[3]. As a result of the efforts to prevent the vertical transmission of HIV, the number of children exposed to HIV is expected to be greater than the number of children infected by it[4]. According to the Brazilian protocol for managing women with HIV, when the rapid test is positive at the time of delivery, a cesarean section is elected, and injectable AZT is administered. If the pregnant woman is living with HIV, adherence to ART and viral load are assessed at 28 weeks of gestation. If the viral RNA load is undetectable and treatment adherence is verified, the choice of delivery route is based on obstetric indication and injectable AZT is not administered. If the viral load is detectable but less than 1000 copies/ml, the delivery route is based on obstetric indication, and injectable AZT is administered. If the maternal viral load is greater than 1000 copies/ml or unknown or treatment adherence cannot be ascertained, a cesarean section is performed, and injectable AZT is administered.

Pregnant women are considered to be at high risk when they are not on ART, did not receive prenatal care, did not receive prophylactic ART during delivery as indicated, started ART after the second half of pregnancy, had acute HIV infection during pregnancy, were breastfeeding, had a detectable or unknown viral load in the third trimester of pregnancy, and were diagnosed with HIV at delivery. In these cases, the treatment regimen will depend on the gestational age of the infant at birth, as follows: 37+ weeks (AZT, lamivudine, and raltegravir for 28 days); between 34 and 37 weeks (AZT, lamivudine for 28 days and nevirapine for 14 days); and under 34 weeks (AZT for 28 days)[5]. According to the current Brazilian protocol, children exposed to HIV must be monitored with four viral load tests (at birth, 14 days after birth, two weeks after prophylaxis, and eight weeks after prophylaxis) and an anti-HIV antibody test at the age of 12 months[5]. This differs from the previous protocol, which recommended performing two viral load tests (the first two weeks after prophylaxis and the second at least six weeks after prophylaxis) and a serological test at 18 months of age[5].

Before March 2021, the period covered by this study, when the protocol was changed, prophylactic AZT was prescribed to all exposed newborns for four weeks. Nevirapine (three doses) was added when the mother did not undergo ART during pregnancy, had an unknown viral load or above 1000 copies/ml in the third trimester, had a sexually transmitted infection (STI), or had a positive HIV test at the time of delivery[5].

Vertical HIV infection continues to be a severe public health issue. The pediatric population is particularly vulnerable to vertical transmission of HIV, which entails a high risk of morbidity and mortality. HIV is a chronic disease with important repercussions on the immature immune system of children. Studying the demographic and clinical characteristics of children vertically exposed to HIV and identifying the risk factors involved can help minimize unfavorable outcomes. In addition to contributing to new strategies to combat the disease, current efforts focus on preventing vertical transmission with appropriate and timely management of pregnant women and newborns. This study aimed to investigate the prevalence of HIV infection and the epidemiological characteristics (demographic and clinical variables, maternal viral load, treatment prescribed to mothers and pregnant women, and outpatient follow-up of exposed children) of children exposed to HIV during pregnancy treated at a reference outpatient clinic over five years.

METHOD

This observational descriptive study included retrospective data from a tertiary pediatric hospital's electronic medical record system in the Brazilian state of Santa Catarina from January 2015 to December 2020. The study was approved by the institution's Research Ethics Committee (certificate no. 4,713,439).

The patients included in the study were either diagnosed with or ruled out as having vertical exposure to HIV. They were treated at the institution's Outpatient Clinic for Infectious Diseases.

A search was made for patients assigned diagnosis code ICD Z20.6 (contact with and suspected exposure to the human immunodeficiency virus). The following data were analyzed: demographics; degree of kinship of the informant; relevant prenatal data; paternal HIV serology; maternal viral load; characterization of prophylaxis when indicated; presence of congenital infections (congenital syphilis, toxoplasmosis or congenital cytomegalovirus); HIV testing of siblings, type of feeding and newborn viral load.

The data were recorded in an Excel table. Descriptive statistics considered frequencies and proportions for categorical variables and means and medians for age. Analyses were performed on SPSS STATISTICS 20.0.0

RESULTS

DEMOGRAPHIC VARIABLES

A total of 678 medical records were assigned the ICD Z20.6 diagnostic code. Fourteen (2.0%) had a confirmed result for HIV infection. Regarding demographic variables, 348 (51.0%) were males aged between 14 days and 21 months at the first outpatient appointment.

In terms of ethnicity, 579 (85.4%) were white. The mother provided the information in 556 (82.0%) medical records. The other variables are described in Table 1.

Table 1: Demographic data (age, sex, and ethnicity) of patients exposed to hiv seen at a tertiary pediatric hospital in the brazilian state of santa catarina from 2015 to 2020

Demographic Characteristics	n	%
Age (N=678)		
• 0 - 2 months	446	65.7%
• 2 - 4 months	210	31.0%
• 6 - 12 months	19	2.8%
• 12+ months	03	0.44%
Sex (N: 678)		
• Male	348	51.3%
• Female	329	48.5%
• Unknown	01	0.1%
Skin color (N: 678)		
• White	579	85.4%
• Black	25	3.7%
• Brown	24	3.5%
• Unknown	50	7.4%

Source: the author (2022)

PRENATAL VARIABLES

A total of 434 mothers (64.0%) were diagnosed with HIV before they became pregnant, 18 (2.65%) were diagnosed at the time of delivery, and 182 (26.8%) were diagnosed during pregnancy. More than half of the latter (56%) were diagnosed in the first trimester of pregnancy.

Four hundred and thirteen mothers (61.0%) had gone to more than six prenatal consultations, 534 (78.7%) had no co-infections, and 68 (10.0%) had syphilis during pregnancy.

A total of 601 (88.6%) pregnant women were on ART. The predominant medications were nucleoside analog reverse transcriptase inhibitors associated with protease inhibitors, with 162 (23.9%) cases. ART was not recorded in 360 (53%) of the analyzed medical records. An undetectable viral load was observed in 414 (61%) of the pregnant women.

Information regarding the serology of the children's parents was included in 662 (97.4%) of the medical records, with negative results in 464 (68.4%) cases.

Use of illicit drugs was denied by 527 (77.7%) pregnant women.

Other prenatal variables are described in Table 2.

DELIVERY VARIABLES

Vaginal delivery was described in 292 (43.0%) cases. Regarding the quantification of viral RNA (viral load), 414 (61.0%) pregnant women had an undetectable load, and 376 (55.4%) received intravenous AZT at the time of delivery.

NEWBORN VARIABLES

Prophylactic ART was administered to 650 (95.8%) newborns immediately after birth; 136 (20.1%) received AZT associated with nevirapine, and 514 (76.8%) were given AZT alone. Sulfamethoxazole-trimethoprim was prescribed to 660 (97.3%) infants exposed to HIV as prophylaxis against pneumocystosis.

Congenital syphilis was described in 30 (4.4%) cases.

The first viral load test was undetectable in 653 (96.3%) patients; the second was undetectable in 606 (89.3%), with 58 (8.6%) losses to follow-up. The serological test performed after 18 months was negative in 381 (56.2%) cases, with 283 (41.7%) losses to follow-up. Other data are presented in Table 3.

Regarding serological screening of siblings, tests were performed in 373 (55.0%) cases, and 15 (4.0%) presented a reactive anti-HIV test.

Six hundred and sixty-seven (98.3%) newborns were given infant formula, three (0.4%) were breastfed, and two (0.29%) were cross-breastfed. Six medical records (0.88%) did not contain information about feeding.

Fourteen (2%) patients exposed to HIV were diagnosed with HIV infection. All were promptly started on ART, and five (35.7%) had their first consultation with a pediatric infectious disease specialist by the age of two months. Five (35.7%) of the confirmed HIV cases had more than six prenatal care visits, six (42.8%) pregnant women were on ART, and three (21.4%) adhered to therapy. Other data are described in Table 4.

DISCUSSION

Vertical exposure to HIV is a relevant public health issue that requires preventive measures and policies to decrease

Table 2. Prenatal variables of patients exposed to hiv seen at a tertiary pediatric hospital in the brazilian state of santa catarina from 2015 to 2020

Prenatal variables	n	%
Use of ART during pregnancy (N: 678)		
• Yes	601	88.6%
• No	44	6.5%
• Unknown	33	4.9%
Adherence to ART (N: 678)		
• Yes	494	72.9%
• No	74	10.9%
• Unknown	110	16.2%
*Maternal ART (N: 678)		
• NRTI+PI	162	23.9%
• NRTI + NNRTI	96	14.1%
• NRTI +INI	39	5.7%
• NNRTI +PI+INI	03	0.5%
• NNRTI +PI	01	0.1%
• Unknown	360	53.0%
• Monotherapy	17	2.5%
Paternal serology (N: 678)		
• Undetectable	464	68.4%
• Detectable	198	29.0%
• Unknown	16	2.3%
Prenatal care visits (N: 678)		
• More than 6	413	61.0%
• 6 visits	55	8.1%
• 5 visits	49	7.2%
• 4 visits	33	4.8%
• 3 visits	26	3.8%
• 2 visits	15	2.2%
• 1 visit	7	1.0%
• None	20	2.9%
• Unknown	60	8.8%
Co-infection during pregnancy (N: 678)		
• No co-infection	534	78.8%
• Syphilis	68	10.0%
• Hepatitis C	7	1.0%
• Hepatitis B	3	0.4%
• Toxoplasmosis	3	0.4%
• Syphilis + toxoplasmosis	1	0.1%
• Syphilis + hepatitis C	1	0.1%
• Syphilis + hepatitis B	1	0.1%
• Unknown	60	8.8%

Source: the author (2022)

Key: *ART: antiretroviral therapy; NRTI: nucleoside analog reverse transcriptase inhibitor; PI: protease inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor; INI: integrase inhibitor

the number of infected children. Vertical transmission occurs in approximately 25% of pregnancies of women living with HIV; however, when preventive measures are implemented, cases of newborn infection drop to 1-2%. Measures to minimize vertical transmission include early diagnosis (during prenatal care), use of ART during pregnancy, introduction of specific care measures during delivery, administration of intravenous AZT at delivery, management of exposed newborns, and feeding the infant with formula[5]. The 2% HIV vertical transmission rate found in this study is in line with the literature.

Only 0.3% of the newborns included in this study were breastfed by their mothers, who did not know they had HIV infection. In Brazil, breastfeeding is contraindicated for babies of mothers living with HIV. The Federal Government provides infant formula free of charge to women in this situation through ordinances 2,104 and 1071 from the Ministry of Health[6]. The state of Santa Catarina provides infant formula for the babies of mothers living with HIV up to one year of age, an essential measure to prevent the vertical transmission of HIV[7].

Most patients in our study were white. However, according to the 2021 National Household Sample Survey (PNAD), 45.0% of Brazilians declared themselves white, 44.8% mixed race, and 9.0% black[8]. A possible explanation for the discrepancy between our study and the PNAD results is that the information about skin color in the medical records was not filled in by the patients but by a third party.

Vertical transmission can occur during pregnancy, childbirth, or breastfeeding[3,9,10]. In our study, 64.0% of the women were diagnosed with HIV before pregnancy, and 56.0% were diagnosed during the first trimester of pregnancy. The data found are promising since vertical transmission increases with delays in maternal diagnosis due to the reduced time of use of prophylactic ART. Diagnosis at the time of delivery considerably increases the possibility of transmission since the viral load is high in cases of recent infection and breast milk[11]. Condoms play an essential role, regardless of the serological status of the partners, during puerperium and breastfeeding as a way to prevent the vertical transmission of HIV and other STIs[12]. The distribution of condoms is a significant public health measure that impacts the vertical transmission of HIV and other STIs. The Brazilian Ministry of Health recommends that treatment for pregnant women living with HIV should include combinations of three antiretroviral drugs[13]. However, 17 (2.5%) pregnant women included in our study used only one antiretroviral drug. It is pertinent to ask whether they were unaware of the names of all the medications used or whether the prescribed regimen was discontinued due to the presence of significant side effects. Given the retrospective nature of the study, we could not verify these possibilities. The World Health Organization (WHO) recommends a minimum of eight prenatal care visits. There is an increase in the number of maternal deaths when only four visits are held[14]. The Brazilian Ministry of Health recommends a minimum of six prenatal care visits[13]. In our study, 21.9% of the pregnant women attended less than six prenatal visits, which hampered early diagnosis and timely initiation of treatment for HIV or other STIs. The explanations for the lack of adequate prenatal care include the fact that some women were homeless (it is estimated that there were approximately 1,000 homeless people in the city of Florianópolis in 2017)[15], delays in pregnancy diagnosis, and the lack of public policies to encourage attendance to prenatal care visits. Pregnant women are a population of interest for serological monitoring due to the risks of vertical transmission. In Brazil, between 2014 and 2017, the prevalence of STIs and syphilis during pregnancy was

Table 3: Results of viral load and serological tests of patients exposed to hiv seen at a tertiary pediatric hospital in the brazilian state of santa catarina from 2015 to 2020

Results	n	%
First viral load test (N: 678)		
• Undetectable	653	96.3%
• Detectable	14	2.0%
• Unknown	11	1.6%
Second viral load test (N: 678)		
• Undetectable	606	89.3%
• Detectable	14	2.0%
• Unknown	58	8.6%
Serological test (N: 678)		
• Undetectable	381	56.2%
• Detectable	14	2.0%
• Unknown	283	41.7%

Source: The author (2022)

estimated at 3.12% and 2.46%, respectively[11]. In this study, 10.0% of the pregnant women and 4.4% of the newborns had congenital syphilis. One possible explanation for this difference is the increase in diagnosed cases of disease caused by the broader availability of rapid tests in healthcare clinics in Santa Catarina[16]. Another possibility is the higher detection rate in Santa Catarina compared to other states, according to the 2021 Syphilis Epidemiological Report. Preventing congenital syphilis is essential since it is a severe condition that can lead to fetal death, adversely affect the child's health, and increase the risk of vertical transmission of HIV[17].

The risk of vertical transmission of HIV increases with fewer than six prenatal visits, lack of adequate prophylactic care to pregnant women, and when the first consultation with a specialist takes place more than two months after birth[18]. Regarding newborns diagnosed with HIV, we found that 35.8% of pregnant women had more than six prenatal visits, 42.8% were on ART, 21.4% adhered to ART, and 35.7% of newborns were taken to a specialist within two months of birth. These findings suggest that there is still room for interventions and strategies to decrease the rate of vertical transmission of HIV.

Vertical transmission of HIV is multifactorial, and prophylactic measures are required to minimize it. Our findings indicate that much has to be done since delays in HIV diagnosis hinder prevention. It is essential to support mothers living with HIV and strengthen prevention efforts against HIV infection for women of childbearing age, pregnant women, and HIV-negative women postpartum.

This study presents the limitations inherent to the retrospective design. The authors recommend organizing prospective studies to better demonstrate reality.

The rate of vertical HIV infection found in this study is in line with the literature. No significant difference was associated with newborn gender, and most mothers attended prenatal care visits as recommended by the Brazilian Ministry of Health. There

Table 4. Characteristics of patients vertically exposed to hiv and diagnosed with hiv infection seen at a tertiary pediatric hospital in the brazilian state of santa catarina from 2015 to 2020

Characteristics	n	%
Age at first prenatal care visit (N: 14)		
• 0-2 months	5	35.7%
• 2-4 months	3	21.4%
• 4-6 months	1	7.1%
• 6-12 months	3	21.4%
• 12+ months	2	14.2%
Skin color (N: 14)		
• White	12	85.7%
• Black	2	14.3%
Relationship (N: 14)		
• Mother	9	64.3%
• Parents	2	14.2%
• Institution	2	14.2%
• Father	1	7.1%
Time of maternal diagnosis (N: 14)		
• During pregnancy	4	28.5%
• Before pregnancy	5	35.7%
• At delivery	1	7.1%
• Puerperium	1	7.1%
• Unknown	3	21.4%
Use of ART during pregnancy (N: 14)		
• Yes	6	42.8%
• No	6	42.8%
• Unknown	2	14.2%
Adherence to ART during pregnancy (N: 14)		
• Yes	3	21.4%
• No	5	35.7%
• Unknown	6	42.8%
Paternal serology (N: 14)		
• Undetectable	5	35.7%
• Detectable	3	21.4%
• Unknown	6	42.8%
Substance use during pregnancy (N: 14)		
• No	8	57.2%
• Crack	2	14.2%
• Tobacco	2	14.2%
• Cocaine	1	7.1%
• Unknown	1	7.1%
Prenatal care visits (N: 14)		
• 6+	5	35.8%
• 6 visits	0	0%
• 5 visits	2	14.2%
• 4 visits	1	14.2%
• 3 visits	1	7.1%
• 2 visits	1	7.1%
• 1 visit	2	7.1%
• Unknown	2	14.2%
Other STI (N: 14)		
• No	7	50.0%
• Syphilis	3	21.4%
• Hepatitis C	2	14.2%
• Unknown	2	14.2%

Source: The author (2022)

Key: ART: antiretroviral therapy; STI: sexually transmitted infection

was a predominance of cases of maternal HIV diagnosed before pregnancy. Less than half of the pregnant women with infants with HIV infection were on ART or adhered to therapy; just over a third attended more than six prenatal care visits; and the infants diagnosed with HIV attended visits with a specialist within six months of birth. It is essential to provide prophylactic care to HIV-negative women and information to women and pregnant women living with HIV about adherence to treatment as a way of minimizing the risks of future infection and its consequences.

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