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Original Article

Factors that affect mother-to-child HIV transmission at a university hospital in southern Brazil

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ABSTRACT

Introduction: The prevention strategies for MTCT of HIV proposed by the World Health Organization (WHO) and other agencies have significantly reduced the number of infected children, child morbidity and mortality associated with HIV, and have improved maternal health. However, the detection rate of pregnant women with HIV in Brazil significantly increased in the last decade10.

Objective: To evaluate factors that may interfere in mother-to-child transmission (MTCT) of human immunodeficiency virus (HIV).

Methods: A historical cohort study with a sample of 299 HIV-infected mothers and their newborns who delivered at the Obstetric Center of the Hospital de Clínicas de Porto Alegre, southern Brazil, from January 2010 to December 2014.

Results: Of the 299 newborns of HIV-infected mothers, 3.7% (n = 11) were infected. Of those, 90.9% (n = 10) were born by cesarean section; 90.9% (n = 10) had ≥ 37 weeks; 54.6% (n = 6) received zidovudine starting within the first 4 hours after birth; and 45.4% (n = 5) received zidovudine and nevirapine. Four women whose newborns were infected with HIV had syphilis during pregnancy (36.4%). Poor adherence to highly active antiretroviral therapy (HAART) ($p < 0.003$), viral load ≥ 1000 copies/mL or ignored in the third trimester ($p < 0.000$), and CD4 count < 500 cells/mm^3 in the third trimester ($p < 0.046$) were significantly associated with an increased risk of MTCT.

Conclusions: Lack of control of risk factors may contribute to unfavorable rates of MTCT of HIV.

Keywords: *Risk factors; infectious disease transmission; vertical transmission; acquired immunodeficiency syndrome*

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In the absence of a preventive intervention, the risk of human immunodeficiency virus (HIV) transmission in utero or during delivery is 15 to 30%, increasing to 24 to 42% through breastfeeding[1]. In 1994, Connor et al.[2] demonstrated that a regimen of zidovudine (ZDV) reduced risk of mother-to-child transmission (MTCT) of HIV of 67.5%. Subsequently, several studies have shown that combination therapy during pregnancy, cesarean section (indicated when maternal viral load after 34 weeks ≥ 1000 copies/mL), and interruption of breastfeeding reduce the rate of MTCT of HIV to less than 2%[3-7]. Despite the implementation of these measures, MTCT of HIV remains a challenge to global public health[7].

The prevention strategies for MTCT of HIV proposed by the World Health Organization (WHO) and other agencies have significantly reduced the number of infected children, child morbidity and mortality associated with HIV, and have improved maternal health[8,9]. However, the detection rate of pregnant women with HIV in Brazil significantly increased in the last decade[10]. In 2006, the rate was 2.1 cases per 1,000 live births, rising to 2.7 in 2015, an increase of 28.6%. The southern region has the highest detection rate, approximately 2.2 times higher than the average rate in Brazil[10].

The state of Rio Grande do Sul is at the top of the national ranking with an HIV detection rate of 10.1 cases per 1,000 live births, as reported in the notifiable diseases information system (Sinan). Porto Alegre was the capital with the highest detection rate in 2015, with 22.9 cases per 1,000 live births[10].

This study aimed to analyze risk factors associated with MTCT of HIV in order to contribute to the improvement of actions that seek to reduce the transmission rate in the city of Porto Alegre.

METHODS

A retrospective cohort study of HIV-positive mothers and their newborns whose delivery occurred in the Obstetric Center of the Hospital de Clínicas de Porto Alegre (HCPA) from January 2010 to December 2014. Data collection was conducted between June and October 2015 based on medical records. This study was approved by the Ethics Committee of the HCPA (protocol no. 140568).

The study included 323 women initially, but the following were excluded: five women whose confirmatory HIV test, after the rapid test, was negative, 17 women whose children were followed in another city, and two women who had stillbirths and did not undergo serologic testing for HIV.

Women's identification data were collected such as age, color, nationality, marital status and level of education.

The following variables were analyzed: use of highly active antiretroviral therapy (HAART), therapy adherence, sexually transmitted diseases, smoking, drugs, prenatal care, quantification of viral load and T-cell count (CD4 count), mode of delivery, time of the rupture of membranes, birth weight, gestational age, Apgar score, and lactation.

HAART adherence was considered good when HIV-positive women took at least 95% of prescription drugs (40), an amount that ensures the inhibition of HIV replication. The frequency of withdrawal of medications at the pharmacy and the maternal viral load measured by laboratory tests were considered parameters for good or bad adherence[11].

Regarding mode of delivery, the Obstetric Center of HCPA follows the current guidelines of the Brazilian Ministry of Health, which states that when the maternal viral load after 34 weeks is < 1000 copies/mL, vaginal delivery is recommended, preferably without amniotomy, episiotomy, or instrumentation, according to obstetric conditions. However, when the maternal viral load after 34 weeks is ≥ 1000 copies/mL or unknown, elective cesarean section is recommended after the 38th week of gestation[11].

Breastfeeding is contraindicated in HIV-positive women, as well as cross-lactation (another nursing mother breastfeeding the child), mixed feeding (breast milk and infant milk formula), and use of human milk with home pasteurization. In the present study, all children received infant milk formula until 6 months of age[11].

As recommended by the Brazilian Ministry of Health, zidovudine (ZDV) syrup should be used for four weeks (28 days) after birth[11]. Newborns started receiving ZDV syrup in the delivery room, immediately after birth[11]. An oral suspension form of nevirapine in combination with ZDV was administered to newborns whose mothers were diagnosed with HIV at delivery, did not use HAART during prenatal care, had a viral load > 1000 copies/mL in the last trimester of pregnancy, or with syphilis during pregnancy[12].

The children were followed at an outpatient clinic until the definition of their HIV status. In our study, children were considered non-infected when they had two viral load tests with undetectable results and/or HIV tests (enzyme-linked immunosorbent assay, ELISA) with non-reactive results after 18 months[11].

Statistical analysis was performed using SPSS statistical software, version 18.0. In all analyses, a p-value ≤ 0.05 was considered statistically significant. Anonymity and privacy of patients, according to the recommendations of the Guidelines and Regulatory Norms Involving Human Subjects of the Brazilian National Health Council Resolution no. 466/12, were guaranteed.

RESULTS

From January 2010 to December 2014, 299 mothers whose infants borned at the Obstetric Center of HCPA, were followed to confirm or exclude the diagnosis of HIV. The MTCT rate during the study period was 3.7% – 11 cases in 299 live births (Table 1).

The epidemiological characteristics of the HIV-positive women included in the study are described in Table 2. There was a predominance of mothers aged 21 to 39 years (81.8%, n = 9), of black color (63.6%, n = 7), married (90.9%, n = 10), from Porto Alegre (81.8%, n = 9), and all of them were Brazilians. Regarding level of education, only 9.1% (n = 1) had higher education. Among the mothers whose newborns were infected with HIV, 54.6% (n = 6) had less than six prenatal care visits, and 90.9% (n= 10) showed rupture of membranes < 4 hours and gestational age ≥ 37 weeks (Table 3).

Table 1: Prevalence of mother-to-child HIV transmission at a university hospital in Porto Alegre, Brazil, from 2010 to 2014.

Total		Newborns infected with HIV		Newborns not infected with HIV	
n	%	n	%	n	%
299	100.0	11	3.7	288	96.3

Table 2: Sociodemographic characteristics of HIV-positive mothers at a university hospital in Porto Alegre, Brazil, from 2010 to 2014.

	Children infected with HIV (n = 11)		Children not infected with HIV (n = 288)		Total (n = 299)		p-value
	n	%	n	%	n	%	
Age							
≤ 20 years	2	18.2	36	12.5	38	12.7	0.792*
21-39 years	9	81.8	238	82.6	247	82.6	
≥ 40 years	0	0.0	14	4.9	14	4.7	
Total	11	100.0	288	100.0	299	100.0	
Color							
White	3	27.3	193	67.0	196	65.6	0.003**
Brown	1	9.1	37	12.8	38	12.7	
Black	7	63.6	58	20.2	65	21.7	
Total	11	100.0	288	100.0	299	100.0	
Level of education							
Middle school§	5	45.4	155	53.8	160	53.5	0.749**
High school§§	5	45.4	99	34.4	104	34.8	
Higher education§§§	1	9.2	34	11.8	35	11.7	
Total	11	100.0	288	100.0	299	100.0	
Marital status							
With a partner	10	90.9	275	95.5	285	95.3	0.497**
Without a partner	1	9.1	13	4.5	14	4.7	
Place of birth							
Porto Alegre	9	81.8	196	68.5	205	69.0	0.547**
Countryside	2	18.2	90	31.5	92	31.0	
Total	11	100.0	286	100.0	297	100.0	

*Fisher's exact test; **Pearson's chi-square test; §Middle school incomplete and complete; §§High school incomplete and complete; §§§Higher education incomplete and complete.

Table 3: Risks to mother-to-child HIV transmission associated with maternal exposure and therapy adherence.

	Newborns infected with HIV (n = 11)		Newborns not infected with HIV (n = 288)		Total (n = 299)		p-value
	n	%	n	%	n	%	
No. of prenatal visits							
≤ 1 visit	2	18.2	32	11.1	34	11.4	0.669**
2-5 visits	4	36.4	91	31.6	95	31.7	
≥ 6 visits	5	45.4	165	57.3	170	56.9	
Total	11	100.0	288	100.0	299	100.0	
Rupture of membranes							
< 4 hours	10	90.9	230	80.0	240	80.3	0.659**
≥ 4 hours	1	9.1	56	19.4	57	19.1	
Unknown	0	0.0	2	0.6	2	0.6	
Total	11	100.0	288	100.0	299	100.0	
Mode of delivery							
Cesarean section	10	90.9	183	63.5	193	64.5	0.063**
Vaginal delivery	1	9.1	105	36.5	106	35.5	
Total	11	100.0	288	100.0	299	100.0	
Gestational age							
< 37 weeks	1	9.1	71	24.7	72	24.1	0.409**
≥ 37 weeks	10	90.9	217	75.3	227	75.9	
Total	11	100.0	288	100.0	299	100.0	

**Pearson's chi-square test.

An undetectable HIV viral load in the third trimester (47.8%, n = 143) and a CD4 count ≥ 500 cells/mm^3 (43.2%, n = 126) ($p < 0.046$) significantly reduced MTCT of HIV, as well as good adherence to HAART (52.5%, n = 157) ($p < 0.003$) and use of the full scheme for MTCT prevention (90.4%, n = 264) ($p < 0.002$). We found that 36.4% (n = 4) of the women whose newborns were infected with HIV did not use HAART during prenatal care because they were diagnosed with HIV only at delivery through rapid testing. Furthermore, 36.4% (n = 4) women presented reactive VDRL results ($p < 0.013$), 63.6% (n = 7) had a HIV viral load ≥ 1000 copies/mL in the third trimester ($p < 0.001$), and none of them had an undetectable HIV viral load. Four women were diagnosed with HIV at birth and had no viral load (Table 4).

Regarding the characteristics of the HIV-infected newborns associated with MTCT (3.7%, n = 11), 63.6% (n = 7) were female, 81.8% (n = 9) weighed ≥ 2500 grams, 72.7% (n = 8) had appropriate gestational age, and 100.0% (n = 11) did not require intubation (Table 5). There was no statistically significant difference.

All newborns (100.0%, n = 299) received either ZDV orally (81.9%, n = 245) or ZDV and nevirapine (18.1%, n = 54) orally starting within the first 4 hours of life and lasting for four weeks[13]. Only one uninfected newborn was breastfed, although all mothers were instructed not to breastfeed, and all newborns received infant milk formula until they completed six months.

Table 4: Risks to mother-to-child HIV transmission associated with maternal exposure and therapy adherence.

	Newborns infected with HIV (n = 11)		Newborns not infected with HIV (n = 288)		Total (n = 299)		p-value
	n	%	n	%	n	%	
CD4 count – third trimester							
< 500 cells/mm^3	8	72.7	111	38.5	119	39.8	0.046**
≥ 500 cells/mm^3	3	27.3	124	43.1	127	42.5	
Ignored	0	0.0	53	18.4	53	17.7	
Total	11	100.0	288	100.0	299	100.0	
Viral load – third trimester							
Undetectable	0	0.0	143	49.7	143	47.8	0.001**
< 1000 copies/mL	4	36.4	51	17.7	55	18.4	
≥ 1000 copies/mL	7	63.6	52	18.0	59	19.7	
Ignored	0	0.0	42	14.6	42	14.1	
Total	11	100.0	288	100.0	299	100.0	
Maternal HAART							
Complete	7	63.6	263	91.3	270	90.3	0.002**
Incomplete§	4	36.4	25	8.7	29	9.7	
Total	11	100.0	288	100.0	299	100.0	
HAART adherence							
Good	1	9.1	157	54.5	158	52.8	0.003**
Bad	10	90.9	131	45.5	141	47.2	
Total	11	100.0	288	100.0	299	100.0	
IV ZDV during labor							
Yes	7	63.6	239	83.0	246	82.3	0.099**
No	4	36.4	49	17.0	53	17.7	
Total	11	100.0	288	100.0	299	100.0	
VDRL test							
Reactive	4	36.4	32	11.1	36	12.0	0.012**
Non-reactive	7	63.6	256	88.9	263	88.0	
Total	11	100.0	288	100.0	299	100.0	

**Pearson's chi-square test; §Highly active antiretroviral therapy (HAART) was considered incomplete when pregnant women did not use it during prenatal care. They were diagnosed with HIV only after a rapid test in the delivery room. IV ZDV, intravenous zidovudine; VDRL, Venereal Disease Research Laboratory.

Table 5: Newborn characteristics associated with mother-to-child HIV transmission at a university hospital in Porto Alegre, Brazil, from 2010 to 2014.

	Newborns infected with HIV (n = 11)		Newborns not infected with HIV (n = 288)		Total (n = 299)		p-value
	n	%	n	%	n	%	
Sex							
Female	7	63.6	137	47.6	144	48.2	0.460**
Male	4	36.4	151	52.4	155	51.8	
Total	11	100.0	288	100.0	299	100.0	
Weight							
< 2500 grams	2	18.2	59	20.5	61	20.4	0.999**
≥ 2500 grams	9	81.8	229	79.5	238	79.6	
Total	11	100.0	288	100.0	299	100.0	
Gestational adequacy							
Adequate	8	72.7	203	70.4	211	70.6	0.855**
Excessive	0	0.0	8	2.8	8	2.7	
Inadequate	3	27.3	77	26.8	80	26.7	
Total	11	100.0	288	100.0	299	100.0	
Intubation							
Intubated	0	0.0	14	4.9	14	4.7	0.983**
Non-intubated	11	100.0	274	95.1	285	95.3	
Total	11	100.0	288	100.0	299	100.0	
Antiretroviral therapy							
ZDV	6	54.5	239	83.0	245	81.9	0.031*
ZDV + NVP	5	45.5	49	17.0	54	18.1	
Total	11	100.0	288	100.0	299	100.0	

*Fisher's exact test; **Pearson's chi-square test. NVP, nevirapine; ZDV, zidovudine.

DISCUSSION

In the present study, the rate of MTCT of HIV was 3.7%, almost twice as the target (2%) set by the Regional Validation Committee for the elimination of MTCT of HIV and congenital syphilis, created by the Pan American Health Organization (PAHO), of which Brazil is a participating country[8]. There have been many efforts to reduce MTCT of HIV[11] in Brazil. However, according to our study, low adherence to HAART was significantly related to increase MTCT[11].

A higher prevalence of HIV-positive newborns of mothers with lower levels of education has been found, which could mean that they are less aware of the importance of adherence to HAART and prenatal care. We found a significant association between HIV-positive newborns and self-declared black mothers[11].

WHO estimates that more than 2 million pregnant women are infected with syphilis and HIV per year worldwide. Syphilis during pregnancy is associated with an increased risk for MTCT. Our study found that 36.4% (4/11) mothers with syphilis had children infected with HIV ($p < 0.013$)[8,12].

For those women who did not receive prenatal care and had no previous diagnosis of HIV, rapid testing allowed the adoption of measures to prevent MTCT. Although these measures have been implemented, 36.4% of women with HIV-infected newborns were diagnosed with HIV in the delivery room. Thus, incomplete prophylaxis scheme was significantly associated with increased MTCT ($p < 0.002$).

Controlling viral factors is important to decrease the rate of MTCT of HIV. In our study, poor adherence to HAART ($p < 0.003$), viral load ≥ 1000 copies/mL or ignored in the third trimester ($p < 0.001$), and CD4 count < 500 cells/mm^3 ($p < 0.046$) in the third trimester were significantly related to increased MTCT[14,15]. Evidently, better results will only be achieved with early diagnosis of HIV, careful monitoring, and adherence to prenatal care. The lack of detection of HIV infection during prenatal care represents a wasted opportunity to prevent MTCT. Appropriate prenatal care helps HIV-positive pregnant women understand their disease, improves adherence to the recommendations of health professionals, and facilitates the identification and treatment of diseases

that increase MTCT, such as syphilis. The rate of MTCT of HIV will be similar to that of developed countries when all HIV-positive pregnant women have access and adhere to prenatal care and HAART.

Although this study had limitations due to its retrospective design, we obtained important information to improve prenatal monitoring and MTCT control. The use of illicit drugs may have not been identified in those patients who did not receive appropriate prenatal care. This could influence the effect of HAART and, consequently, the control of the viral parameters that affect MTCT. This is one of our challenges to avoid MTCT of HIV. Lack of control of risk factors may contribute to unfavorable rates of MTCT of HIV.

Conflicts of interest

The authors declare no conflicts of interest.

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