Clinical aspects of co-infection by HIV and syphilis in pregnancy and exposure in newborn intended at Pediatric Hospital of Santa Catarina

Aspectos clínicos da coinfecção por HIV e sífilis na gestação e da exposição de recém-nascidos atendidos em Hospital Pediátrico de Santa Catarina

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ABSTRACT

Introduction: Sexually transmitted infections frequently affect pregnant women and, consequently, newborns. HIV and syphilis are vertically transmitted to children and co-infection requires special attention due to its clinical implications. **Objective:** To describe clinical aspects of HIV/syphilis coinfection during pregnancy and the exposure of newborns to infections treated at a pediatric reference hospital in Santa Catarina between 2015 and 2020. **Methods:** Observational, descriptive study, secondary to a line of research "Epidemiological description of children exposed to HIV" from January 2015 to December 2020 in a tertiary pediatric hospital in Santa Catarina. **Results:** 678 medical records were analyzed with ICD Z.206 (contact with and exposure to HIV), in which 71 (10.5%) newborns were exposed to HIV and Syphilis co-infection. Of these, 37 (52.1%) were male, 14 (19.7%) confirmed a diagnosis of HIV and 30 (42.2%) of congenital syphilis. Of the co-infected pregnant women, 38 (53.5%) were diagnosed with HIV prior to pregnancy, 53 (74.6%) used ART and 40 (52.1%) used harmful substances. Furthermore, 34 (46.4%) pregnant women had a minimum number of 6 prenatal consultations, 35 (49.3%) had vaginal births and 29 (40.8%) had undetectable HIV RNA quantification at the time of delivery. HIV prophylaxis for newborns occurred in 66 (92.9%) of cases. **Conclusion:** It is concluded that the studied population was mostly made up of pregnant women who were diagnosed with HIV infection prior to pregnancy. Of these, the majority were using ART, but the minority carried out the minimum number of consultations recommended by the Ministry of Health. Regarding newborns, the majority received HIV prophylaxis.

Keywords: Pediatrics. Pregnancy complications, infectious. Infectious disease transmission, vertical. Syphilis, congenital.

RESUMO

Introdução: As infecções sexualmente transmissíveis afetam frequentemente gestantes e, consequentemente, os recém-nascidos (RN). O vírus da imunodeficiência humana (HIV) e a sífilis são transmitidos verticalmente para as crianças e a coinfecção requer atenção especial por suas implicações clínicas. **Objetivo:** Descrever aspectos clínicos da coinfecção HIV/sífilis na gestação e da exposição de RN às infecções atendidos em um hospital de referência pediátrica em Santa Catarina entre 2015 e 2020. **Métodos:** Estudo observacional, descritivo, secundário à linha de pesquisa "Descrição epidemiológica de crianças expostas ao HIV" no período de janeiro de 2015 a dezembro de 2020, em um hospital pediátrico terciário de Santa Catarina. **Resultados:** Foram analisados 678 prontuários com Classificação Internacional de Doenças — CID Z.206 (contato com e exposição ao HIV), nos quais 71 (10,5%) RN foram expostos à coinfecção HIV e sífilis. Destes, 37 (52,1%) eram do sexo masculino, 14 (19,7%) confirmaram diagnóstico de HIV e 30 (42,2%) de sífilis congênita. Das gestantes coinfectadas, 38 (53,5%) possuíam diagnóstico do HIV prévio à gestação, 53 (74,6%) usaram terapia antirretroviral (TARV) e 40 (52,1%) utilizaram substâncias nocivas. Ainda, 34 (46,4%) gestantes obtiveram o número mínimo de seis consultas pré-natais, 35 (49,3%) realizaram partos vaginais e 29 (40,8%) possuíam quantificação RNA-HIV não detectável no momento do parto. A profilaxia para o HIV do RN ocorreu em 66 (92,9%) dos casos. **Conclusão:** Conclui-se que a população estudada foi formada, na sua maioria, por gestantes que receberam o diagnóstico de infecção pelo vírus do HIV prévio à gestação. Destas, a maioria estava em uso de TARV, porém a minoria realizou o número mínimo de consultas preconizadas pelo Ministério da Saúde. Com relação aos RN, a maioria recebeu profilaxia ao HIV.

Palavras-chave: Pediatria. Complicações infecciosas na gravidez. Transmissão vertical de doenças infecciosas. Sífilis congênita.

INTRODUCTION

Sexually Transmitted Infections (STIs), including the human immunodeficiency virus (HIV), pose a major global health issue, with significant consequences for maternal and fetal health [1].

HIV is a retrovirus formed by a ribonucleic acid (RNA), transmitted through contact with contaminated blood, transplacentally breastfeeding and, mainly, sexual transmission. However, in children, the main form of contamination is vertical transmission [2]. According to the 2022 Epidemiological Bulletin, 149,591 pregnant women with HIV were reported in Brazil from 2000 to June 2022, 8,323 of which were in 2021 alone [3].

Thereby, antiretroviral therapy (ART) aims to slow the progression of the disease and reduce the risk of transmission to newborns [2]. Several new infections in children can be prevented by pregnant women using ART and prenatal care. However, cases of poor adherence to treatment and lack of knowledge of their own serological status for the virus can harm the results [4].

Congenital syphilis has a high rate of vertical transmission and there is still a possibility of transmission to the fetus through the birth canal, provided that there are genital lesions in the pregnant

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woman [5]. Diagnosis in pregnant women is made during prenatal care, and it is important to carry out timely treatment with penicillin in order to minimize vertical transmission. The lack of treatment or inadequate treatment can lead to serious consequences for the newborn, such as fetal or perinatal death, prematurity, low birth weight and compromise of the cardiovascular, ophthalmological and neurological systems [6].

In Brazil, in 2022 alone, 213,129 thousand cases of acquired syphilis were reported, and 83,034 thousand cases in pregnant women [7]. Additionally, in 2021, 27,019 cases of congenital syphilis were reported in the country [7]. Therefore, it is a preventable disease, a simple and curable diagnosis, but with a high prevalence in Brazil [6].

In a retrospective cross-sectional analytical study carried out in Porto Alegre in 2016, the prevalence ratio of vertical HIV transmission, in the unadjusted analysis, was 2.1, in the group of newborns of co-infected pregnant women[8].

Given the importance of the subject, goals proposed by the Ministry of Health (MS) have emerged to reduce vertical mother-to-child transmission (MTCT) of HIV and/or syphilis, in which it is expected to reduce the rate of vertical HIV transmission to ≤ 2% by 2025 and reduce the incidence of congenital syphilis to < 0.5 cases per 1,000 live births by 2030. In addition, among the goals, the MS intends to expand coverage to ≥ 95% of pregnant women who undergo at least one test for HIV and syphilis during prenatal care; increase coverage of adequate treatment for HIV and syphilis, aiming for at least 95% of pregnant women with these diseases to receive treatment; expand access to rapid testing for the diagnosis of HIV and syphilis during prenatal care, both for pregnant women and their partners [9].

OBJECTIVE

Therefore, based on the prevalence and severity of exposure to syphilis and HIV coinfection, the study aims to describe the clinical aspects of HIV and syphilis coinfection during pregnancy and also the exposure of newborns treated at a pediatric referral hospital in Santa Catarina between 2015 and 2020.

METHODS

This is an observational, descriptive study, secondary to a line of research "Epidemiological description of children vertically exposed to HIV in a tertiary pediatric hospital in Santa Catarina"[10], in which de Souza et al.[10] retrospectively evaluated 678 medical records of retrospective data collection in a tertiary pediatric hospital in Santa Catarina from January 2015 to December 2020. Approved by the institution's CEP under (CAAE) 46274621.3.0000.5361.

The initial research search was performed using ICD Z.206 (contact with and exposure to the human immunodeficiency virus - HIV) and, based on these data, only cases of children exposed to HIV and syphilis coinfection were selected for the present study. Thus, the following were analyzed: demographic data of the newborn (sex, skin color and institutionalization); prenatal data (time of maternal HIV diagnosis, use of harmful substances by the pregnant woman, number of prenatal consultations, other simultaneous coinfections); type of delivery; paternal HIV serology; maternal HIV treatment (use of ART, type of ART, medication adherence); quantification of maternal HIV RNA at the time of delivery; use of zidovudine (AZT) in the pregnant woman at the time of delivery; implementation of HIV prophylaxis for the newborn.

All patients during the proposed period treated at the institution's infectious disease outpatient clinic who had exposure to HIV and syphilis due to mothers with co-infections during pregnancy were included in the study.

The data were recorded in an Excel table, descriptive statistics were performed with frequency and percentages for categorical variables, mean and median for the age variable, supporting software was Statistical Package for the Social Sciences — SPSS STATISTICS 20.0.0®.

RESULTS

The study analyzed 678 medical records classified with ICD Z.206, of which 71 (10.5%) showed exposure to HIV and syphilis due to maternal coinfection. Among these, the average age at the start of follow-up in the outpatient clinic was 59 days of life, with a minimum value of 23 days and a maximum of 196 days.

In Table 1, regarding the variables sex and skin color, we observed that 37 (52.1%) were male and 60 (84.5%) were white. Regarding the origin of the study participants, 58 (81.7%) lived with their parents, and there is no specific data on the residence of the other participants. The other variables are described in **Table 1.**

Regarding the maternal characteristics of patients exposed to HIV and syphilis, 38 (53.5%) mothers were diagnosed with HIV before pregnancy, and two were diagnosed at the time of delivery. Of the 71 medical records, 53 (74.6%) described the use of ART by the pregnant woman, the most common being Nucleoside Analogue Reverse Transcriptase Inhibitors (NRTIs) and Non-Nucleoside Analogue Reverse Transcriptase Inhibitors (NNRTIs), found in 12 (16.9%) cases. Furthermore, it is worth mentioning that in 66.20% of the cases, the data regarding the type of ART used by the pregnant women were not known. Regarding adherence to Antiretroviral

Table 1. Demographic data of patients vertically exposed to HIV and Syphilis due to maternal co-infection treated at the Santa Catarina Pediatric Hospital between 2015 and 2020.

Variables	n	%
Gender		
Male	37	52.1
Female	34	47.9
Skin color*		
White	60	84.5
Mixed-race	5	7.1
Black	2	2.8
Not informed	4	5.6
Live with parents		
No	58	81.7
Yes	13	18.3

Source: The authors, 2023.
*Note: IBGE 2022 skin color category.

Therapy, 33 (46.5%) used medication regularly. No data were obtained on adequate maternal treatment for syphilis (**Table 2**).

Regarding paternal data (43.7%), they did not know their HIV and syphilis serological status and did not have data on treatment.

Furthermore, the use of harmful substances by pregnant women was described in 40 (52.1%) of the cases, the most frequent being crack, with 15 (21.1%) users in the study.

Regarding prenatal care, 30 (42.2%) medical records showed more than 6 consultations, where other infections were identified simultaneously in 3 cases, namely hepatitis B (1 case), hepatitis C (1 case) and toxoplasmosis (1 case).

About the type of childbirth, 35 (49.3%) pregnant women had vaginal delivery. In 29 (40.8%) cases, HIV RNA quantification was undetectable at the time of delivery. Intravenous AZT was administered as prophylaxis to minimize vertical transmission of HIV to the newborn in 30 (42.2%) pregnant women. After delivery, AZT alone was used in approximately 30 (42%) of the newborns. Even so, prophylaxis with AZT + NVP was administered in 34.8% of the newborns exposed to vertical transmission of HIV.

Even so, of the 71 newborns exposed to coinfection, vertical transmission of HIV occurred in 14 (19.7%) cases and vertical transmission of syphilis occurred in 30 (42.2%) patients. Of these 14 patients with HIV, 3 (21.4%) had coinfection with syphilis (**Table 3**).

Table 2. Prenatal data from mothers of patients vertically exposed to HIV and Syphilis due to maternal co-infection treated at the Santa Catarina Pediatric Hospital between 2015 and 2020.

Variables	n	%
Timing of maternal HIV diagnosis		
Prior to pregnancy	38	53.5
During prenatal care	19	26.8
During childbirth	2	2.8
Not informed	12	16.9
Use of TARV		
Present	53	74.6
Absent	7	9.9
Not informed	11	15.5
Type of TARV		
ITRN-ITRNN	12	16.9
ITRN-IP	8	11.3
ITRN-INI	4	5.6
Desconhecido	47	66.2
Adherence to TARV		
Yes	33	46.5
No	12	16.9
Not informed *	9	12.7
Not applicable†	17	23.9
Paternal HIV diagnosis		
Negative	26	36.6
Positive	14	19.7
Unknown	31	43.7
Substance abuse by pregnant women		
Crack	15	21.1
Tabacco	12	16.9
Alcohol	8	11.3
Cannabis	4	5.6
Cocaine	1	1.4
No harmful substances	34	47.9

Source: The authors, 2023.

HIV: human immunodeficiency virus; ART: Antiretroviral therapy. NRTI: nucleoside reverse transcriptase inhibitors; NNRTI: non-nucleoside reverse transcriptase inhibitors; PI: protease inhibitors; INI: integrase inhibitors.

* Pregnant women who received ART, but without information on treatment adherence in their medical records; †Pregnant women who had been diagnosed with HIV, but did not receive treatment or pregnant women whose medical records did not contain information on whether they had received treatment. Therefore, treatment adherence does not apply.

Tabela 3. Characteristics of prenatal care and monitoring of patients vertically exposed to HIV and Syphilis due to maternal co-infection treated at the Santa Catarina Pediatric Hospital between 2015 and 2020.

Variables	n	%
Number of prenatal consultations		
More than 6	30	42.2
6	3	4.2
5	5	7.0
4	6	8.4
3	7	9.9
2	3	4.2
1	4	5.6
No prenatal care	3	4.2
Unknown	10	14.1
Other simultaneous co-infections		
Hepatitis B	1	1.4
Hepatitis C	1	1.4
Toxoplasmosis	1	1.4
None	68	95.8
Type of childbirth		
Vaginal birth	35	49.3
Cesarean section	34	47.9
Not informed	2	2.8
Quantification of maternal HIV-RNA at the time of delivery		
Undetectable	29	40.8
Detectable	7	9.9
Unknown	35	49.3
Intravenous AZT in pregnant women at the time of delivery		
Yes	30	42.2
No	10	14.1
Unknown	31	43.7
Prophylaxis for newborns*		
Yes	66	92.9
AZT	42	63.6
AZT+NVP	23	34.8
Irregular	1	1.5
No	0	0.0
Unknown	5	7.1
Vertical transmission of HIV		
Yes	14	19.7
No	57	80.2
Vertucal transmission of syphilis		
Yes	30	42.2
No	41	57.7

Source: The authors, 2023.

RNA-HIV: ribonucleic acid - human immunodeficiency virus; AZT: zidovudine; NVP: nevirapine; HIV: human immunodeficiency virus

DISCUSSION

Of the 678 medical records evaluated using ICD Z.206, exposure to HIV and syphilis due to maternal coinfection was identified in 71 (10.5%) of them. It was found that 37 (52.1%) were male, similar to that found by Magdaleno et al.,[11] who described 24 (50%) newborns for each gender. This can be explained because the pathologies studied do not have a predilection between the genders for infection, so there are no significantly important statistical differences.

The timing of maternal diagnosis is extremely important for the evolution of the case, as it is related to the risk of vertical transmission, since this increases with delayed diagnosis due to the reduction in the time of use of antiretroviral prophylaxis[1]. The current study showed that 38 (53.5%) pregnant women received the diagnosis prior to pregnancy, unlike the study by Medeiros[12], in which only 22.3% of pregnant women knew the diagnosis previously. Currently, infectious screening tests for STIs such as HIV have been implemented more frequently in routine examinations of the sexually active population. Thus, it is possible that, due to the greater availability of such tests, there is a proportion of women with a diagnosis prior to pregnancy.

According to the Ministry of Health, all pregnant women living with HIV should be treated and use a combination of three antiretroviral drugs along with viral load quantification at 34 weeks to choose the route of delivery. According to the current Brazilian protocol, to be considered low risk for vertical transmission, according to the current PCDT, treatment has to start in the first half of pregnancy, with good adherence and undetectable viral load from the 28th week of gestation [13]. Therefore, in this study, ART was used in only 53 (74.6%) pregnant women, a higher result when compared to that of Acosta et al.[8], in which only 29 (20.3%) underwent treatment during prenatal care[8]. However, the result is still below the MS target of 95% of pregnant women treated[9], requiring raising awareness among mothers with educational campaigns, ensuring easy access to diagnostic tests and treatment, training health professionals, integrating health services and social support for pregnant women to increase HIV treatment coverage during prenatal care.

Comparing the same studies, in this research, paternal HIV diagnosis was found in 14 (19.7%) of the cases, like Acosta et al.,[8] who observed 56 (23.1%) of HIV-positive partners [8]. Vertical transmission occurs in approximately 25% of pregnancies of women living with HIV who do not take adequate prophylaxis; however, with prevention actions, this number can be reduced to 1–2%[14]. Measures to minimize vertical transmission are: early diagnosis (during prenatal care), correct use of ART during pregnancy, specific care during childbirth, intravenous AZT at delivery, management of the exposed newborn and provision of infant formula to the newborn [13].

Concerning the use of harmful substances during prenatal care, 8 (11.3%) used alcohol and 32 (45%) used some type of drug, results similar to those described by Medeiros[12], who found 163 (16%) and 43 (4.2%), respectively. According to studies, the use of alcohol, tobacco or illicit drugs, a lower level of education and the lack of prenatal care are risk factors associated with HIV and syphilis coinfection [8]. The use of illicit substances during pregnancy can have consequences for the conceptus and may even lead to fetal and/or neonatal death. Most children of mothers who use alcohol and other drugs tend to be born prematurely, with low weight for gestational age and needing hospitalization in a neonatal ICU [15].

The Ministry of Health recommends a minimum of 6 prenatal consultations, and a number lower than this is related to an increase in infections among pregnant women [14]. Thirty-three (46.4%) pregnant women had at least 6 prenatal consultations, while according to Medeiros[12], 107 (73,3%) had the minimum recommended. Both studies showed results below expectations, making it necessary to reinforce to mothers the importance of prenatal care, facilitate access to health care, and implement an active search for pregnant women for consultations in order to reach the minimum number of consultations recommended by the Ministry of Health [14]. Therefore, there are several reasons why mothers do not attend such consultations, such as difficulty in getting around, reduced opening hours, lack of awareness and support, financial difficulties, among others. Therefore, it is up to public policies to identify and address such barriers, so that all women receive the minimum recommended care.

There are several preventive measures to minimize vertical transmission to newborns, including the choice of delivery route. In women living with HIV, vaginal delivery may be considered when they have been regularly taking ART since the first half of pregnancy, using antiretrovirals at the time of delivery, and having undetectable HIV RNA quantification or <1,000 copies/mL at the time of delivery [14]. In the study, there were 35 (49.3%) vaginal deliveries and 34 (47.9%) cesarean sections, similar to the 43.9% and 49% of vaginal delivery and cesarean sections, respectively, described by Acosta et al.[8]. It is noted that approximately half of the births were performed by cesarean section, which can be related to the fact that 49.3% of the pregnant women studied had an unknown viral load for the HIV virus. Therefore, was opt for the surgical delivery route, in accordance with the current PCDT, aiming to reduce the risk of vertical transmission of HIV [14].

Regarding the treatment of newborns, at the time data were collected, the treatment protocol used prophylactic AZT for 4 weeks for all newborns exposed to HIV. In cases where: the mother did not use ART during pregnancy, had an unknown viral load or above 1000 copies/ml in the third trimester or still had a reactive result for HIV at the time of delivery, it was necessary to combine AZT with nevirapine (NVP). Currently, in the protocol for the treatment of newborns, it is necessary to assess the risk of vertical transmission. Thus, pregnant women are considered at high risk for vertical transmission if: they do not use ART during prenatal care and at the time of delivery (as indicated); they start ART after the second half of pregnancy; they acquire acute HIV infection during pregnancy; they have a detectable viral load in the third trimester or an unknown viral load; they discover the infection only at delivery. In these situations, the newborn's drug therapy will be according to the gestational age at birth: greater than 37 weeks — AZT, lamivudine and raltegravir for 28 days; between 34 and 37 weeks — AZT, lamivudine for 28 days and NVP for 14 days; and less than 34 weeks — AZT for 28 days[13]. There were 42 (63.6%) newborns using AZT and 23 (34.8%) using AZT + NVP, in agreement with the study by Gonçalves[16], which found 20 (51.2%) monotherapies and 13 (33.3%) combined therapies (AZT + NVP).

The presence of syphilis in pregnant women represents an additional risk for vertical transmission of HIV, regardless of educational level and prenatal care. Newborns exposed to maternal co-infection with syphilis and HIV face a higher risk of vertical transmission of HIV compared to those exposed only to maternal HIV infection [16,17]. Considering that the 71 newborns in the study were exposed to co-infection, vertical transmission of HIV was observed in 14 (19.7%). Interestingly, when compared with the main line of research that originated this study, among the 678 medical records analyzed with exposure to the virus, no cases of vertical transmission of HIV were recorded from mothers who were exclusively HIV-transmitted, without co-infection with syphilis. In other words, the same 14 cases of vertical transmission of HIV were observed in the present study. Unlike the study by Kinikar et al.[18], in which, among new-borns exposed to HIV and syphilis, there was vertical transmission of HIV in 15%, compared to a transmission rate of 3% among those without exposure to syphilis.

Therefore, preventing vertical transmission of syphilis, as well as HIV, is extremely important so that even after the pregnant woman is infected, the newborn can be prevented from becoming infected. Therefore, it is of fundamental importance that after this is necessary, the pregnant woman be monitored by the health teams so that the correct treatment can be administered as quickly as possible. In syphilis, according to the MS protocol, treatment is considered adequate when a pregnant woman begins taking Benzathine Penicillin up to 30 days before delivery. The therapeutic regimen should follow the clinical stage of syphilis, respecting the recommended products between doses. In addition, it is advisable that the pregnant woman's sexual partner be tested and treated, if necessary, to prevent reinfection [14].

In this study, it was found that a minority of women (46%) had already been diagnosed with HIV before pregnancy. However, treatment with ART during pregnancy was identified in the majority of the pregnant women studied, approximately 75%. Even so, a minority of pregnant women attended the minimum number of prenatal consultations recommended by the Ministry of Health. Regarding newborns, the vast majority received HIV prophylaxis. Therefore, early diagnosis is extremely important, associated with quality prenatal care and appropriate treatment in order to achieve medication adherence and consequently reduce vertical transmission. To this end, as indicated previously, public policies are needed that offer high-quality prenatal services, monitor pregnant women and conduct regular assessments to verify adherence to consultations and identify regions that require improvements and greater attention.

Finally, problems related to data quality were found in medical records due to specific limitations of the retrospective research design, such as missing information and incomplete data.

Strengths

The study's strengths include the concordance in comparison with other literature. In addition, it highlights the importance of prevention, early diagnosis and adequate treatment to reduce vertical transmission of HIV and syphilis, highlighting key points for intervention and improvement of maternal and child health care in the context of public health policies.

Limitations

The study suffered from limitations inherent to the retrospective research design, due to failures in filling in information and digitizing medical records and the loss of patient follow-up at the outpatient clinic studied.

CONCLUSION

Therefore, it is concluded that maternal diagnosis prior to pregnancy was prevalent, and most pregnant women received ART during pregnancy, complying with the guidelines of the Ministry of Health to reduce vertical transmission of HIV. The presence of maternal syphilis increased the risk of vertical transmission of HIV, highlighting the need for early diagnosis and adequate treatment during pregnancy. The use of harmful substances during pregnancy and prenatal consultations below the recommended number are still challenges in public health. The importance of early diagnosis and adequate prenatal care is highlighted to reduce vertical transmission of HIV and syphilis.

Approval by the Ethics And Research Committee

The research was approved by the CEP of the Joana de Gusmão Children's Hospital under CAAE 46274621.3.0000.536.

Participation of each author

LKPS: Formal analysis, Conceptualization, Writing – review and editing, Methodology. MJKD: Formal analysis, Conceptualization, Writing – review and editing, Methodology. JKS: Data curation. APC: Writing-project supervision. SMF: Writing-project supervision. ERC: Methodology, Conceptualization, Writing - review and editing, Methodology.

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Conflict of interest

The authors declare that there is no conflict of interest in the study.

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