Human Immunodeficiency Virus infection associated with crack cocaine use: the impact on perinatal transmission among 890 pregnancies in Brazil

Infecção pelo vírus da imunodeficiência humana em associação ao uso de crack: qual o impacto na transmissão perinatal entre 890 gestantes

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ABSTRACT

Introduction: Human Immunodeficiency Virus infection is a prevalent infection occurring during pregnancy. The implementation of a program to screen and prevent vertical transmission is highly important in Public Healthcare. Pregnant crack users could face difficulties to test and adhere to the Highly Active Antiretroviral Therapy. **Objective**: The purpose of this research paper was to investigate whether crack cocaine abuse increases Human Immunodeficiency Virus perinatal transmission rates, as well as to evaluate the risk factors associated with such an increase. **Methods**: Design: A retrospective study. Setting: Department of Obstetrics and Gynecology, General Hospital of Universidade Federal do Paraná. Population: pregnancies of Human Immunodeficiency Virus-positive women who were using crack cocaine (n=64) were compared with that of non-users (n=826) from 2005 to 2013. Prenatal medical records, delivery records, and newborn records were analyzed. Main Outcome Measures: The vertical transmission of Human Immunodeficiency Virus in the group of crack cocaine users was 9.37% (6) *versus* 2.54% (21) among non-users (p=0.009744). **Results**: Over the years of the study, there was a decrease in the vertical transmission rate in non-users, while this number remained constant in the group of users. When analyzing the cases of perinatal transmission, it was found that 83.34% (5) had inadequate prenatal care, and 100% (6) had inadequate Human Immunodeficiency Virus treatment, compared to the group in which there was no vertical transmission, where 65.52% (38) had inadequate prenatal care and 70.86% (41) had inadequate treatment. **Conclusion**: Vertical transmission is higher among crack cocaine users and did not decrease over the years of the study, as occurred among non-users. Trends that explain this increase were non-adherence to adequate prenatal care, Human Immunodeficiency Virus diagnosis during pregnancy, irregular treatment, absence of intrapartum antiretroviral prophylaxis, and vaginal delivery route.

Keywords: HIV. Crack cocaine. Vertical infection transmission. Substance-related disorders.

RESUMO

Introdução: A contaminação pelo vírus da imunodeficiência humana é uma infecção prevalente ocorrida na gravidez. A implantação de um programa de rastreamento e prevenção da transmissão vertical é um campo tão importante na saúde pública. Neste caso, a gestante, usuária de *crack*, pode estar com alguma dificuldade de testagem e adesão à administração da terapia antirretroviral altamente ativa. **Objetivo**: Analisar os casos de gestantes vírus da imunodeficiência humana positivas e usuárias de *crack* atendidas na maternidade do Hospital de Clínicas da Universidade Federal do Paraná entre 2005 e 2013. Propõe-se avaliar se o uso de *crack* aumenta a transmissão vertical do vírus da imunodeficiência humana e, caso isso ocorra, quais seriam os possíveis fatores que explicariam esse aumento. **Métodos**: Trata-se de um estudo retrospectivo e descritivo, com análise de prontuários da obstetrícia (pré-natal), do atendimento ao parto, da ficha de avaliação do recém-nascido e do prontuário de evolução do recém-nato. Foi comparada a taxa de transmissão perinatal de vírus da imunodeficiência humana de usuárias (n=64) e não usuárias de *crack* (n=826) no período de 2005 a 2013. Posteriormente, analisando apenas os casos de uso de *crack*, foram pareados os grupos com e sem transmissão vertical, avaliando condições sociais, condições do recém-nato, tratamento adequado para o vírus da imunodeficiência humana durante a gestação, entre outras variáveis. **Resultados**: A transmissão vertical de vírus da imunodeficiência humana foi de 9,37% em usuárias de *crack* e de 2,54% em não usuárias, com alta significância estatística (p=0,009744). Ao longo dos anos do estudo, houve um decréscimo da taxa de transmissão vertical em não usuárias de *crack*, enquanto nas usuárias esse número permaneceu constante. Nos casos de transmissão vertical, 83,34% das pacientes tiveram um pré-natal inadequado e em 100% o tratamento para o vírus da imunodeficiência humana na gestação foi inadequado em comparação com o grupo no qual não houve transmissão vertical, em que o pré-natal inadequado foi de 65,52% e o tratamento inadequado foi de 70,86%. O uso de adequada profilaxia antirretroviral intraparto se mostrou um dos principais fatores diretamente associados com a proteção contra a transmissão vertical (p=0,065). **Conclusão**: A transmissão vertical de vírus da imunodeficiência humana é maior em usuárias de *crack* e não se mostrou em queda ao longo dos anos do estudo, como ocorreu nas não usuárias. Foram encontradas tendências que explicam esse aumento, por exemplo não adesão ao pré-natal adequado, diagnóstico do vírus da imunodeficiência humana durante a gestação, tratamento irregular, ausência de profilaxia antirretroviral intraparto e via de parto vaginal. Prematuridade e baixo peso ao nascer foram maiores nos recém-natos das usuárias em relação aos índices encontrados na literatura do país. Fica evidenciada a necessidade de atendimento diferenciado para essas gestantes, visto que elas não obedecem às medidas adotadas até o momento para o controle da transmissão vertical.

Palavras-chave: HIV. Crack cocaína. Transmissão vertical de doenças infecciosas. Drogadição.

INTRODUCTION

In 2004, the detection rate of pregnant women with HIV observed in Brazil was 2 cases per one thousand live births, which increased to 2.5 in 2013, indicating an increase of 25%[1]. Brazil was the first

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developing country to implement a countrywide program to prevent HIV vertical transmission. HIV counseling and testing, as well as HAART and infant formula, are provided free of charge to patients. In Brazil, over 95% of women give birth in hospitals, creating a key opportunity for the systematic offering of HIV rapid testing and other interventions aimed at the prevention of mother-to-child transmission (PMTCT)[2].

The use of illicit drugs increased in recent years in Brazil and has become a serious public healthcare problem that also affects pregnant women. Among other drugs, crack cocaine, an inhaled form of cocaine that emerged in the mid-1970s is particularly worrying in an increasingly intense way. According to research conducted by the Brazilian Center for Information on Psychotropic Drugs (CEBRID) in 2001 and 2005, it was found that the use of crack cocaine increased from 0.4–0.7% of the Brazilian population[3,4]. In 2012, the Oswaldo Cruz Brazilian Foundation (FIOCRUZ) surveyed about 25,000 people living in 26 cities in Brazil and estimated that the use of crack cocaine and/or similar drugs was prevalent in 0.81% of the population, which corresponded to 370,000 users in these cities only[5]. Drug use during pregnancy predisposes changes to maternal immune responses with increased viral replication in the cells of the mother's immune system and also of the fetus and newborn[6]. Furthermore, this drug involves specific and serious factors to users, like lack of, or poor, prenatal care causing family, social or obstetric problems, inadequate treatment of HIV, among others[7].

This was a retrospective study that analyzed pregnant women infected with HIV who were crack cocaine users. It was conducted at the Maternity Ward of the General Hospital of Universidade Federal do Paraná (UFPR) between the years 2005–2013 (nine years). This study intends to evaluate the vertical transmission rate and the potential causes of vertical transmission, including social factors. The conditions of the newborns were also analyzed to identify the outcome.

OBJECTIVE

The purpose of this research was to investigate whether crack cocaine abuse increases HIV perinatal transmission rates, as well as to evaluate the risk factors leading to such an increase.

METHODS

This was a retrospective and descriptive study conducted in a tertiary hospital in the State of Paraná, Brazil. First, samples were collected and the records of crack cocaine users were crossed with records of HIV-positive pregnant women who gave birth in the maternity ward of the UFPR General Hospital from 2005–2013. This collection was made with the help of the Epidemiology service – through the analysis of epidemiological data from the National Information System for Notifiable Diseases (SINAN), the Infectology Division in the Pediatrician Sector, and the Social and Psychological Maternity Service, where crack cocaine users received psychological support. Asking about the use of drugs is a planned question at the HIV specialized outpatient center at the Department of Gynecology and Obstetrics, where all the patients of the study were selected. The sample involved 59 women with 64 pregnancies. Six patients had two pregnancies during the study period and were analyzed twice because some of the factors can change from one pregnancy to the other, changing the risk of vertical transmission. Details of sample collection can be seen in **Figure 1**.

Prenatal medical records, delivery records, and newborn records were analyzed. The data observation protocol was carried out: the records to be analyzed in the search of information were the reports containing obstetric data. As for the newborn data, the birth reports, records from the Infectology Division of the Pediatrician Sector, and the results of laboratory tests were observed. Cases of vertical transmission were considered those that had two positive viral loads[8,9]. A minimum of six appointments at the prenatal care outpatient center was defined as good quality prenatal care[10]. When the medical record indicated poor or no treatment (the patient does not use HAART daily), HIV treatment was considered inadequate. The HIV tests shown in the records were done using the ELISA technique and confirmed with Western Blot[11]. Rapid HIV Testing of Women in Labor and Delivery was also used. In the analysis of social factors, patients were divided by per capita income, according to the classification of the Brazilian Institute of Geography and Statistics (IBGE)[12]. Low birth weight is defined as a live-born infant weighing less than 2,500 g, and prematurity was considered to be before the start of the 37th week of pregnancy. This study was submitted to the Human Research Ethics Committee of the General Hospital and was approved. Data were entered in a spreadsheet (Microsoft Excel), then checked, and exported for further statistical analysis. The descriptive analysis of the qualitative variables was performed using frequencies and percentages. To investigate the association between these variables, the chi-square test and Fisher's exact were used. Statistical analysis was performed using IBM SPSS Statistics.

RESULTS

Between January 2005 and December 2013, 885 HIV-positive pregnant women (890 pregnancies) gave birth in the maternity ward of the UFPR General Hospital and 59 pregnant women were crack cocaine users, with 64 pregnancies (7.19%). The vertical transmission of HIV occurred in 6 neonates (9.37%) from crack cocaine users and 21 (2.54%) from non-users (p=0,009744) (**Figure 2**). While analyzing the incidence of perinatal transmission within these two groups over the time of the study, a decrease in the vertical transmission rate among crack cocaine non-users, primarily because of the use of Antiretroviral Therapy (ART) during pregnancy can be observed. This trend is not followed by the group of users, who have non-decreasing transmission rates and variable rates over time. It was observed that the use of crack cocaine in HIV-positive pregnant women increased from 2005–2007, then began to decline until 2013. But there were three vertical transmission peaks in 2006, 2009, and 2012 (**Figure 3**).

Considering the positive HIV crack cocaine users only, cases of vertical transmission and cases without vertical transmission were matched. Social factors, adherence to prenatal care and treatment, and perinatal outcome were analyzed. The results are shown in **Table 1**.

Comparing these two groups, we observed that in cases without vertical transmission, the considered adequate prenatal care rate was

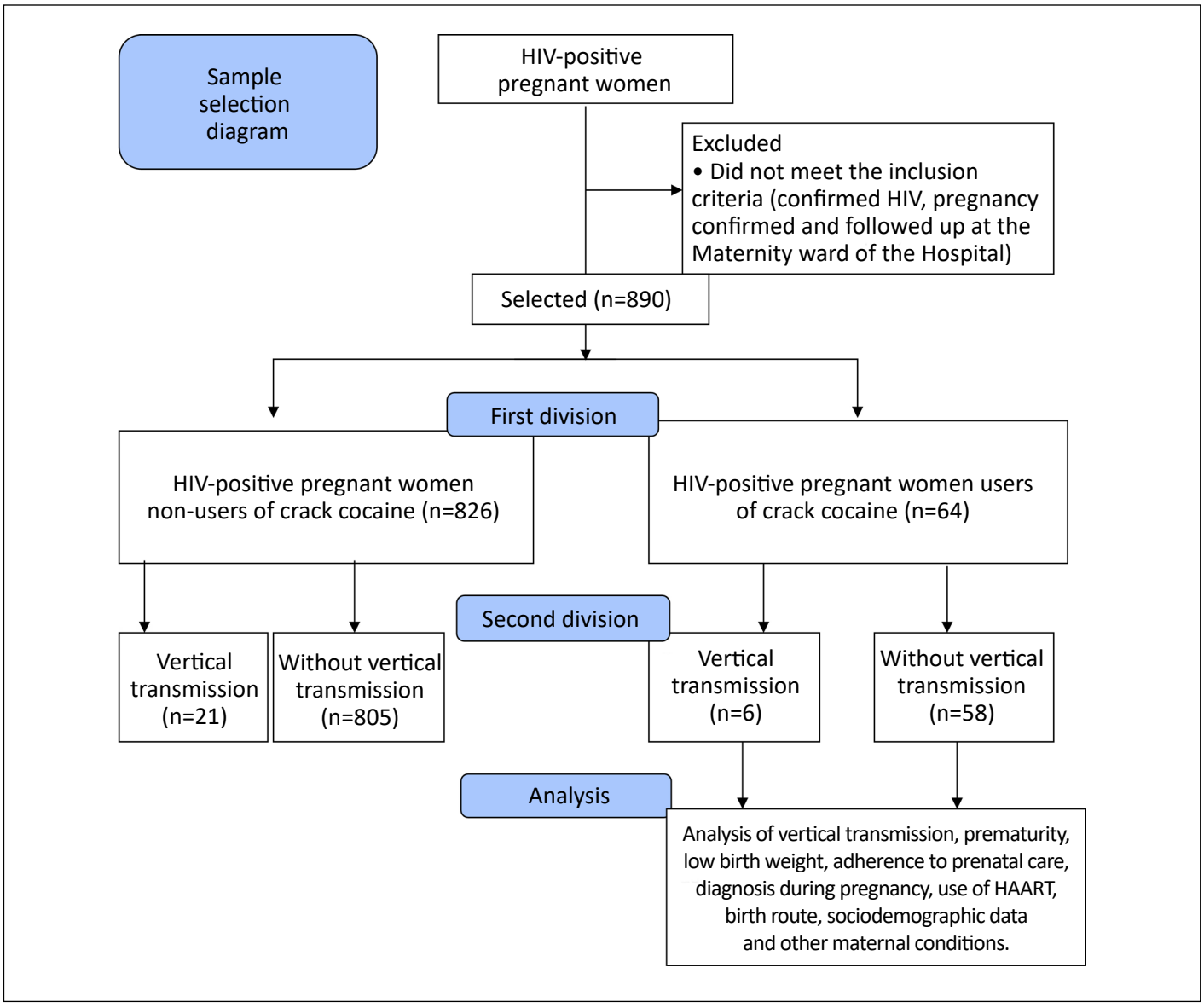


Figure 1 – Sample selection diagram (according to CONSORT).

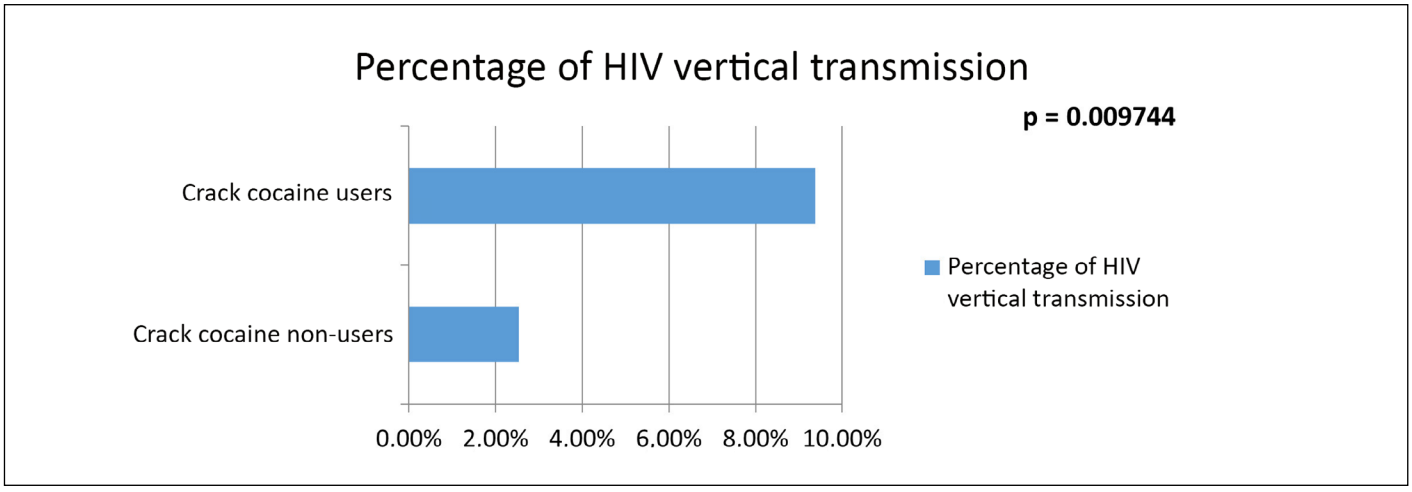


Figure 2 – Vertical transmission of HIV in crack cocaine users and non-users analyzed among 890 HIV-positive pregnant women treated at the Clinic Hospital of the Federal University of Paraná – Maternity in the 2005–2013 period.

two times higher. Moreover, prenatal care was inadequate in 83.34% (5/6) of the vertical transmission cases and HIV was diagnosed during pregnancy in 50% (3/6) of them. Additionally, after evaluating the entire sample of HIV-positive pregnant women who were crack cocaine users, it was found that 39% (26/64) of patients had HIV infection diagnosed during the current pregnancy. Among those, 56% (15/26) had the disease diagnosed in the third trimester of pregnancy, losing the opportunity of starting treatment at the correct time. Small for gestational age neonates were 4/6 (66%) among crack cocaine users. The use of intrapartum antiretroviral prophylaxis tends to be considered as a protective factor against perinatal transmission of HIV (p=0.065).

To evaluate the impact of prenatal care, the group with adequate care was paired with the group with inadequate care. The results are shown in **Table 2**.

When prenatal care attendance along with social factors was analyzed, it was observed that the attendance rate of HIV-positive pregnant women who were crack cocaine users and had a steady partner, steady employment, and a per capita income above "vulnerable" was not modified. However, it was observed that for both groups (with adequate and inadequate prenatal care), the per capita income of more than 50% (47/64) of the pregnant women were classified as extremely poor, poor, or "vulnerable" (up to 77 dollars/month. The rate of preterm births among all patients was 30%

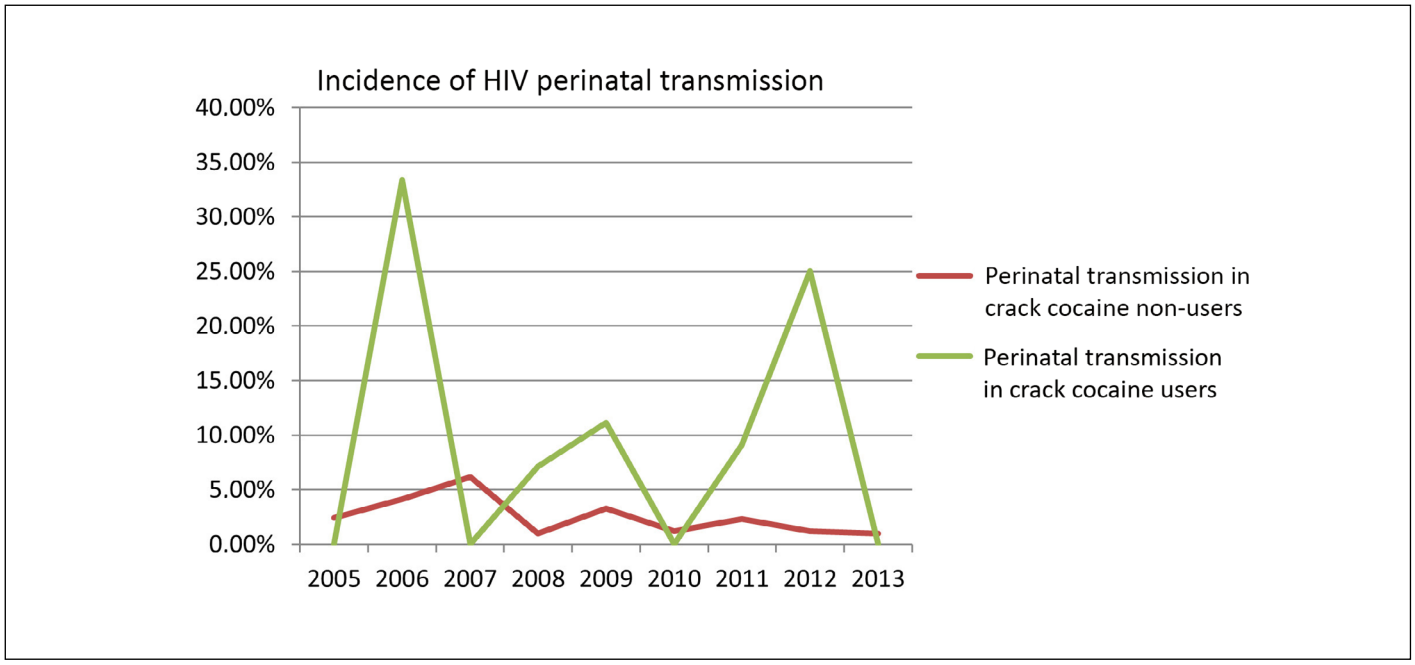


Figure 3 – Incidence of perinatal transmission of HIV in crack cocaine users and non-users analyzed among 890 HIV-positive pregnant women treated at the Clinic Hospital of the Federal University of Paraná – Maternity in the 2005–2013 period.

Table 1 – Comparison of cases with and without vertical transmission.

Variables	Cases without vertical transmission % (n=58)	Cases with vertical transmission % (n=6)	p-value
Adequate prenatal care (6 or more appointments)	34.48 (n=20)	16.66 (n=1)	0.6543
HIV diagnosis during pregnancy	39.31 (n=23)	50 (n=3)	0.6800
Irregular or absent treatment	70.86 (n=41)	100 (n=6)	0.3231
Intrapartum antiretroviral prophylaxis	94.82 (n=55)	66.66 (n=4)	0.0651
Prematurity	30 (n=34)	16.66 (n=1)	0.667
Low birth weight	39.65 (n=23)	66.66 (n=4)	0.391
Vaginal birth	21.46 (n=1)	50 (n=3)	0.3663

Table 2 – Comparison of cases with and without adequate prenatal care.

Variables	Adequate prenatal care %	Inadequate prenatal care %	p-value
Vertical transmission	4.76 (n=1)	11.62 (n=5)	0.6543
Steady partner	57.14 (n=12)	56.09 (n=23)	1
Steady employment	23.52 (n=4)	23.07 (n=9)	1
Per capita income above "vulnerable"	41.66 (n=7)	44.18 (n=10)	0.3249
Prematurity	23.09 (n=5)	30.23 (n=13)	0.7684
Low birth weight	38.09 (n=8)	44.18 (n=19)	0.6432

(18/64), and low birth weight was 42% (27/64). When paired with the attendance of prenatal care, the results show that there was no statistical significance between receiving or not receiving prenatal care and premature birth or low birth weight.

Despite the use of the HAART protocol, 74% (47/64) of all HIV-positive pregnant women who were crack cocaine users did not use HAART or did not use it properly. The route of birth was vaginal birth in 26.00% (16) of the sample. Among the cases of vertical transmission, 50% (3/6) of childbirths were vaginal, and in 33.34% (2/6), intravenous zidovudine (AZT) intrapartum was not used because the mother was already in the second stage of labor or in labor before their arrival to the hospital.

The association with other drugs was common, affecting 76% (49/64) of pregnant women. The use of crack cocaine and cigarette smoking was the most common association among the subjects (20%), followed by crack cocaine, smoking, and alcohol consumption (18.8%) – licit drugs that are easily accessible. Association with cocaine only, alcohol only, and marijuana only had the lowest rates, with 4.7, 3.1, and 1.6%, respectively.

The maternal viral load in two cases of vertical transmission was 4688 and 8763 copies. In the other four cases, the viral load was unknown. In both cases with known viral load, a cesarean section was the chosen method of birth. Of the mothers who transmitted HIV, two had hepatitis C, two had syphilis, and two had urinary tract infection during pregnancy. In this study, there were no cases of vertical transmission of HIV through breastfeeding because lactation was inhibited after birth.

DISCUSSION

In 2012, 370,000 children were infected with HIV worldwide, more than 1,000 per day. This number is alarming and shows that there are still a lot of infections that need to be prevented despite the progress that has already been made[13].

In this study, we found 64 cases of pregnancies among HIV-positive women who confirmed they were crack cocaine users, which corresponds to 7.19% of pregnancies of HIV-positive women who gave birth in the UFPR General Hospital between 2005 and 2013. The hospital where the study was conducted is a state reference for high-risk pregnancy, showing a possible bias in the results of the study, as a high percentage of crack cocaine users and vertical transmission of HIV was observed compared to data from other sites.

The study showed that crack cocaine users had four times more maternal-fetal transmission of HIV compared to non-users (9.37 and 2.54%) (p=0,009744). The incidence of vertical transmission among non-users decreased during the period under study, while the incidence did not decrease among users, being variable and remaining at high rates. There has been a downward trend of vertical transmission in Brazil as a whole: 35.7% in the last ten years (2004-2013). However, there is no data in the literature regarding the incidence of vertical transmission of HIV among crack cocaine users.

The mother's immunity is critical in defining vertical transmission and it is reduced in cocaine and crack cocaine users, both because of the lack of adherence to treatment by the patients and because of factors associated with the interaction between drugs and the virus[14]. It is known that the drug stimulates the replication of HIV and the reduction of blood cells, and changes the production of cytokines in the body and the expression of HIV in the mononuclear phagocytic system cells[15-17].

In this study, most of the pregnant women using crack cocaine did not use HAART correctly. In the cases analyzed, in 100% of the cases of mother-to-child transmission, treatment was inadequate or absent, confirming the importance of careful attention being paid to these mothers, with a focus on improving treatment outcomes. As for the correct treatment, the attendance of prenatal care is important and shows that the patient is interested in having the disease treated. In this study, only 16.66% (1) of the vertical transmission cases had received proper prenatal care, which can be another factor associated with the use of crack cocaine and the high rate of vertical transmission.

The viral load of pregnant women in which there was vertical transmission was unknown in four of the six cases and it was over 1,000 in the other two cases. Half of all births were by the vaginal route and half were by cesarean section. The Brazilian Consensus for attention to HIV-positive pregnant women suggests that the vaginal birth route is possible provided that the viral load, tested at a higher gestational age, 34 weeks, is below 1,000 copies. If above 1,000 copies or unknown (as in the case of all pregnant women in which vertical transmission occurred), an elective cesarean section should be considered[12]. In addition, all HIV-positive pregnant women, regardless of the type of childbirth, should receive intravenous AZT from the beginning of labor or at least 3 hours before an elective cesarean section. AZT should be maintained until the umbilical cord is clamped[13]. In this study, 94.82% (55) of pregnant women with no maternal-fetal transmission of HIV received intravenous AZT compared to 66.66% (4) among the cases of vertical transmission. This reinforces the literature regarding that intrapartum AZT is an important protective factor in preventing vertical transmission[18].

Regarding the outcomes of newborns, 30% (18) were born prematurely and 42% (27) had low birth weight. The overall incidence of prematurity in the country in 2013 was 11.7%, and low birth weight was 8%[19]. According to a study of 7698 pregnant women[20], HIV per se is not a risk factor for prematurity and low birth weight. The high rate of such conditions in the cases analyzed confirms the previous studies conducted with crack cocaine users and their pregnancies, which highlight 'crack babies'[21] as generally being premature, low-weight, and having intrauterine growth restriction[22] since this drug easily crosses the placenta. A retrospective study[23] conducted with 1,693,197 women identified a higher risk of disorders related to the placenta, gestational hypertension, preeclampsia, and eclampsia in cocaine users compared to non-users. Because prematurity and low birth weight are factors that increase the risk of HIV vertical transmission, it can be assumed that one of the risk factors of crack cocaine use in pregnancy involves these outcomes in newborns.

The perspective is to make a case-control study comparing all the factors analyzed in this paper, among crack cocaine users and non-users with a large sample of patients, to see if there is statistical significance. In addition, further studies are needed to assess the social and behavioral factors of these women, so that they can implement meaningful and specific measures to attract them to the prenatal visits.

Strengths

This study confirms the importance of testing and HAART therapy adherence for HIV vertical transmission prevention among pregnant women and the importance of prenatal multidisciplinary care being offered to pregnant women who are crack users, among which vertical transmission has increased.

Limitation

The small sample and the fact that the study was retrospective could be seen as a limitation. A large sample and a case-control comparative study could show more statistical significance based on the findings.

CONCLUSION

With the significant increase in the rate of HIV vertical transmission among crack cocaine users combined with no decrease in this rate in recent years, it is noticeable that these patients are not participating in and receiving comprehensive care offered by the healthcare system. A better form of alternative care and follow-up must be considered for this group. Possibly more visits, creating specific outpatient drug programs, and referral to social and psychological care could be effective alternatives. It is also necessary to prevent pregnant women from arriving at the hospital during the second stage of labor, having their babies outside the hospital, and not receiving the correct number of prenatal visits, resulting in an unknown viral load. Finally, while pregnant women who are crack cocaine users alone should receive special care, when combined with being HIV-positive, special care should be mandatory to help reduce the rate of vertical transmission in this population.

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Approval by the Human Research Ethics Committee

This study was submitted to the Human Research Ethics Committee of Universidade Federal do Paraná General Hospital and was approved on 01.25.2015, No. 956 271.

Participation of each author

NSC: Data curation, Formal Analysis, Writing – original draft, Writing – review & editing. CCVB: Data curation, Formal Analysis, Writing – original draft, Writing – review & editing. JR: Data curation, Formal Analysis, Writing – original draft, Writing – review & editing. ARPM: Data curation, Formal Analysis, Writing – original draft, Writing – review & editing. CFM: Data curation, Formal Analysis, Writing – original draft, Writing – review & editing. EGT: Data curation, Formal Analysis, Writing – original draft, Writing – review & editing. RLS: Data curation, Formal Analysis, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors report no conflict of interest.

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