# Epidemiologic and clinical characteristics of pregnant women living with HIV/AIDS in a region of Southern Brazil where the subtype C of HIV-1 infection predominates


## ABSTRACT

Southern Brazil has the highest prevalence rate of AIDS in the country and is the only region in the Americas where HIV-1 subtype C prevails. **Objective:** We evaluated the epidemiologic and clinical characteristics of pregnant women living with HIV/AIDS in the South region of Santa Catarina, Brazil. **Methods:** All pregnant women with HIV infection attending the obstetric outpatient clinic of Criciúma, State of Santa Catarina, in 2007 (n = 46) were invited to participate. Data of 36 eligible participants were obtained through a standardized questionnaire. **Results:** The great majority were young, with a steady partner, low family income, low education level and referring early first sexual intercourse. Many reported use of illicit non-injecting drugs (55.5%) and unprotected sex with partners that were HIV-positive (57.7%), injecting drug user (22.2%), male inmate (19.4%), truck driver (13.8%), with history of sexually transmitted disease (11.1%) or men who have sex with men (MSM) (2.8%). Most (66.7%) of the participants had their HIV diagnosis done during the pregnancy, 7 (19.4%) had a previous history of HIV mother-to-child transmission. Therapy based on highly active antiretroviral therapy (94%) was initiated at 19.3 weeks on average and 33% showed irregular antiretroviral adherence. **Conclusion:** These results confirm previous data on HIV epidemiology in Brazil and suggest that the women partners' sexual behavior and unprotected sexual intercourse are important aspects of HIV epidemic. Additional efforts in education, prophylaxis and medication adherence are needed.



**Keywords:** AIDS; serodiagnosis; HIV infections; pregnancy; HIV-1 subtype C; Southern Brazil.


## INTRODUCTION

The human immunodeficiency virus (HIV) infection has a worldwide distribution causing a devastating public-health problem, especially in developing countries.[1,2] According to the World Health Organization, Brazil has a concentrated HIV epidemic with an estimation of about 600,000 adults living with HIV/AIDS. In this country, from 1980 to June 2009, 544,846 cases of acquired immunodeficiency syndrome (AIDS) were notified to the Brazilian Ministry of Health. By June 2009, 26,057 AIDS cases had been reported in Santa Catarina State, Southern Brazil. In 2008, 14 cities of Santa Catarina were among the 50 Brazilian cities with the highest numbers of AIDS cases, and the city of Criciúma, located in the south of the state, had an prevalence rate of 40.1 cases per 100,000 residents.[3]

HIV epidemic may actually constitute a myriad of multiple sub-epidemics, both at a subpopulation and geographic level, with significant variation within and between them.[4,5] In Brazil, a constant change in HIV epidemic regarding gender infection ratio, age of infection and risk behavior have been described. The HIV infection in female population has increased and nowadays women have been infected in the proportion of 1.5 men to 1 woman.[6] Brazil's AIDS treatment program guarantees free access to highly active antiretroviral therapy (HAART) for all people living with HIV/AIDS and in need of treatment, including all pregnant women and their newborns.[7,8]

HIV-1 subtype C is the most prevalent worldwide, accounting for more than 56% of all infections.[9] One of the most important features of the current Brazilian AIDS epidemic seems to be the spread of the HIV-1 C in Southern Brazil.[10,11] Partial HIV sequences of the *pol, gag* and *env* genes were obtained from 26 pregnant women studied in the present work, and HIV-1 subtypes at *pol* were


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C in almost 80% of the isolates.[12] Despite this increasing incidence of HIV-1 C infection in cities of Southern Brazil, and the high risk of mother-to-child transmission (MTCT) during pregnancy few studies have examined the epidemiological factors associated with the HIV infection in pregnant women in these Brazilian regions. To investigate this question, a cross-sectional study was carried out to describe the socioeconomic, reproductive, clinical, sexual and risk behavior characteristics associated with HIV infection in a Southern Brazilian cohort of pregnant women.

## *MATERIAL AND METHODS*

### Population and sample collection

All pregnant women with HIV-1 diagnosis based on the algorithm proposed by the Brazilian Ministry of Health,[6] who received care in the Municipal HIV/AIDS Programs of Criciúma, serving the city and nearby villages at the coastal area of Santa Catarina State from January to December 2007, were invited to participate in this study. After explaining the purpose of the study, those who accepted to participate signed an informed consent form and had the socioeconomic, reproductive, clinical, sexual and risk behavior variables assessed by a standardized interview questionnaire elaborated by the National Program of Sexually Transmitted Disease of the Brazilian Ministry of Health. Face-to-face interviews were conducted during pregnancy by trained personnel supervised by the research team. Socioeconomic and demographic data were collected including age, marital status, race, education level, family income and working status; maternal variables were number of pregnancies, including the current one, number and kind of deliveries. The medical care variables were age at the first prenatal visit, time of HIV diagnosis, antiretroviral (ARV) use and adherence, lymphocyte T cell counts (CD4 and CD8) and viral load. Sexual and risk behavior data obtained included number and characteristics of sexual partners, history of prior sexually transmitted infections, frequency of condom use, history of sex for money, drug use, and age at the first sexual intercourse. After the interview, blood samples were collected and stored for future serological and molecular assays. All participants had their medical records examined to abstract clinical and laboratory data. This study was approved by the Ethics Committees of the *Universidade do Extremo Sul Catarinense* (protocol number 642/2007).

### Data analysis

The clinical and behavioral data were stored in Epidata and exported for final analysis with the SPSS Program version 14.0. Categorical variables were initially described with absolute and relative frequencies.

## *RESULTS*

### Demographic and socioeconomic characteristics of pregnant women infected with HIV in southern Brazil

Of the 46 eligible participants, HIV-infected pregnant women receiving prenatal care from January to December 2007, 36 (78.2%) agreed to participate. Age ranged of 17-37 years (Table 1). Just over 77.8% identified themselves as white. Most (86.1%) were married or cohabiting with a steady partner, 61% had less than 8 years of formal education and 83.4% were not formally employed. Forty-seven percent identified themselves as housewives, and two (5.6%) as female commercial sex worker. The average family income per month was low; 8.3% had no income and 77.2% had an income of less than three minimum wages approximately (Table 1).

### Reproductive characteristics of HIV infected pregnant women

The total number of pregnancies reported by the interviewed women was 101, with 97 deliveries (60.8% vaginal delivery and 39.2% elective cesarean) and four miscarriages (3.96%). Most of them (77.8%) had a previous pregnancy, and the total number of pregnancies reported by each woman ranged from 1 to 7 with an average of 2.81 (Table 2). Considering the more recent pregnancies (in the year of 2007) we observed that 69.4% of all births were by cesarean delivery. The HIV diagnosis was carried out during pregnancy in 24 women (66.7%), 15 during the current and 9 in previous pregnancies. However, it was found that 20 (55.5%) women were aware of their HIV status before the previous pregnancy (Table 2) and 7 mothers had a previous history of MTCT of HIV. One of these had two gestations where HIV transmission could not be prevented (data not shown).

### Clinical, immunological and HIV status of pregnant women

The mean age of the participants at the time of HIV diagnosis was 23.3 years. The average gestational age at first prenatal care visit was 17.8 ± 8.3 weeks, but the average duration from HIV-1 infection since diagnosis was 40.1 months (Table 3). About 25% of them had their HIV diagnosis confirmed more than five years ago. Mean gestational age at the beginning of antiretroviral therapy was 19.3 ± 8 weeks (Table 3). Considering the last laboratory data obtained few weeks before delivery, around 33.3% of the women had undetectable plasma viremia, 30.5% had 1,000 to 10,000 RNA copies/mL, and 13.9% showed viral load between 10,000 and 100,000 copies/mL. Mean T CD4 lymphocyte was 612 cells/mm$^3$ and 77.8% of the women had T CD4 counts above 350 cells/mm$^3$. T CD8 cell counts ranged from 336 to 2,817 cells/mm$^3$ and with an average of 1,196 ± 586 cells/mm$^3$. Most participants (77.8%) were

*Table 1. Demographic and socioeconomic characteristics of pregnant women living with HIV/AIDS in Southern Brazil*

| Pregnant HIV-positive women (n=36) | | |
|---|---|---|
| **Age (years)** | **n** | **(%)** |
| 17 - 19 | 4 | 11.1 |
| 20 - 24 | 13 | 36.1 |
| 25 - 29 | 11 | 30.6 |
| > 30 | 8 | 22.2 |
| Average (SD) | 26.1 (5.37) | |
| Mode | 24 | |
| **Race** | | |
| White | 28 | 77.8 |
| Black | 5 | 13.9 |
| Mixed (parda) | 3 | 8.3 |
| **Marital status** | | |
| Steady partner (married or cohabiting) | 31 | 86.1 |
| Single | 5 | 13.9 |
| **Education level** | | |
| Never attended school | 1 | 2.8 |
| 1 - 3 years | 4 | 11.1 |
| 4 - 7 years | 17 | 47.2 |
| 8 - 11 years | 13 | 36.1 |
| > 12 years | 1 | 2.8 |
| **Working status or occupation** | | |
| Housewife | 17 | 47.2 |
| Unemployed | 9 | 25.0 |
| Employed | 6 | 16.6 |
| Pensioner or social assistance | 2 | 5.6 |
| Female commercial sex worker | 2 | 5.6 |
| **Family income (MW)[a]** | | |
| 0 | 3 | 8.3 |
| < 1 minimum wage | 5 | 13.9 |
| 1 - 2.9 minimum wages | 21 | 58.3 |
| 3 - 5.9 minimum wages | 7 | 19.5 |

[a]The Brazilian national minimum wage is adjusted annually. Nowadays it is R$ 510 (which corresponds to $294.83 per month).

*Table 2. Reproductive characteristics of pregnant women living with HIV/AIDS in South of Santa Catarina, Brazil*

| Pregnant HIV-infected women | | |
|---|---|---|
| **Reproductive characteristics** | **n** | **(%)** |
| **Number of lifetime pregnancies (n = 101)** | | |
| 1 | 8 | 22.2 |
| 2 | 10 | 27.8 |
| 3 | 9 | 25.0 |
| ≥ 4 | 9 | 25.0 |
| Average (SD) | 2.81 (1.64) | |
| Mode | 2 | |
| **Mode of delivery (all deliveries n = 97)** | | |
| Vaginal delivery | 59 | 60.8 |
| Elective C-section | 38 | 39.2 |
| **Mode of delivery (most recent pregnancy n = 36)** | | |
| Vaginal delivery | 11 | 30.6 |
| Elective C-section | 25 | 69.4 |
| **Diagnosis of HIV status (n = 36)** | | |
| Made before gestation | 12 | 33.3 |
| Made during previous pregnancy | 9 | 25.0 |
| Made during current pregnancy | 15 | 41.7 |
| Aware of their HIV status since before the previous pregnancy | 20 | 55.5 |

classified as HIV infected, and 8 (22.2%) as patients with AIDS defined by T CD4 cells < 350 cells/mm$^3$ (Table 3).

Almost 95% of the pregnant women received either ARV treatment or prophylaxis for prevention of vertical transmission. In most cases the ARV regimen consisted of a nucleoside reverse transcriptase inhibitor (NRTI) backbone (zidovudine + lamivudine) with nevirapine or protease inhibitor (PI) (lopinavir/ritonavir or nelfinavir) (Table 3). Two women (5.6%) began only zidovudine (ZDV) monotherapy rather late. One started at 37 weeks due to a late HIV diagnosis. The other woman, a crack addict with history of irregular antiretroviral adherence, started the monotherapy only during labor (after our staff could find her). She knew about her HIV diagnosis since 2004 during a previous pregnancy.

*Table 3. Clinical, immunological and HIV status of pregnant women living with HIV/AIDS in Southern Brazil*

| | n | (%) |
|---|---|---|
| **Gestational age at first antenatal visit** | | |
| 7 - 14 (weeks) | 14 | 38.9 |
| 15 - 26 | 15 | 41.7 |
| 28 - 31 | 5 | 13.8 |
| 37 | 2 | 5.6 |
| Average (SD) | 17.8 (8.3) | |
| **Time since HIV diagnosis** | | |
| 1 - 20 (months) | 15 | 41.7 |
| 21 - 60 | 12 | 33.3 |
| 61 - 120 | 8 | 22.2 |
| > 121 | 1 | 2.8 |
| Average (SD) | 40.1 (34.4) | |
| **Gestational age at the initiation of therapy** | | |
| 7 - 14 (weeks) | 12 | 33.3 |
| 15 - 26 | 17 | 47.3 |
| 27 - 31 | 5 | 13.8 |
| 37 | 1 | 2.8 |
| During labor | 1 | 2.8 |
| Average (SD) | 19.3 (8) | |
| **Viral load (copies/mL)[a]** | | |
| Undetectable | 12 | 33.3 |
| < 1,000 | 7 | 19.5 |
| 1,000 - 10,000 | 11 | 30.5 |
| > 10,000 | 3 | 8.3 |
| > 100,000 | 2 | 5.6 |
| Not available | 1 | 2.8 |
| Average | 10,984 | |
| **Laboratorial and clinical status** | | |
| **CD4 cells count x $10^3$/mL** | | |
| > 350 | 28 | 77.8 |
| 201 - 350 | 4 | 11.1 |
| < 200 | 4 | 11.1 |
| Average (SD) | 612.5 (380.7) | |
| **Immunological classification[b]** | | |
| Non AIDS | 28 | 77.8 |
| AIDS | 8 | 22.2 |
| **Antiretroviral regimen[c]** | | |
| ZDV/3TC + LPV/r or NFV | 30 | 83.3 |
| ZDV/3TC + NVP | 4 | 11.1 |
| ZVD only | 2 | 5.6 |
| **Treatment adherence[d]** | | |
| Regular | 24 | 66.7 |
| Irregular | 12 | 33.3 |

[a]Defined as HIV RNA level less than 80 copies/mL of plasma.
[b]Based on TCD4 cell count < 350 cells x $10^3$/mL.
[c]ZDV, zidovudine; 3TC, lamivudine; LPV/r, ritonavir-boosted lopinavir; NFV, nelfinavir; NVP, nevirapine.
[d]Antiretroviral adherence based on the Physician and Pharmacist's information.

Her newborn was the only case of HIV MTCT among this group of pregnant women in 2007. Poor adherence to ARV therapy was reported by 33.3% of cases. Nevertheless, no cases of serious HIV related complications or death of mothers were verified after two years of follow-up after delivery (data not shown).

## Sexual characteristics and prevalence of risk factors to HIV infection

Among HIV-infected pregnant women the mean age at first sexual intercourse was 15.2 years (Table 4). In this group of women a prior history of injecting drug use, blood transfusion and occupational accidents were not associated with HIV infection (Table 4). The most important mother's exposure category was heterosexual contact with partners with risk factors for HIV/STD infection. A high percentage of women reported having 3-10 partners over lifetime (57.7%). Also, a high percentage had a steady sex partner with at least one of the following characteristics: HIV-infected (57.7%), injecting drug user (IDU) (22.2%), male inmate (19.4%), truck driver (13.8%), with history of sexually transmitted disease (STD) (11.1%) and men who have sex with men (MSM) (2.8%) (Table 4).

In relation to unprotected sex with steady partner during the last month, a significant percentage of women (41.7%) had never used condoms, 22.2% of them reported consistent use and 36.1% used them irregularly. Considering lifelong sexual intercourse with a steady partner, 55.5% reported never having used condoms, and almost 40% had used them irregularly. Moreover, no use and irregular use with casual partners were reported by 27.8% and 30.5% of pregnant women, respectively.

In relation to drug-related HIV risk behaviors, 55.5% of women had been exposed to non-injecting drugs, including licit and illicit drugs. Cigarette use was reported in 18 cases (50%), alcohol abuse in 9 (25%), crack cocaine in 5 (13.8%), marijuana or cocaine in 3 cases (8.3%). Moreover, almost 50% of women reported the use of illicit drugs either isolated or in combination (Table 4).

*Table 4. Sexual and risk behavior characteristics of pregnant women living with HIV/AIDS in Southern Brazil*

| **Age at first sexual intercourse (years)** | **n** | **(%)** |
|---|---|---|
| 11 - 13 | 4 | 11.1 |
| 14 - 16 | 26 | 72.2 |
| 17 - 19 | 6 | 16.7 |
| Average (SD) | 15.2 (1.75) | |
| **Exposure category** | | |
| Sexual | 36 | 100 |
| IDU | 0 | 0 |
| Blood or blood product | 0 | 0 |
| Occupational accident | 0 | 0 |
| Tattoo | 1 | 2.8 |
| **Number of lifetime partners** | | |
| 1 - 2 | 10 | 27.8 |
| 3 - 5 | 12 | 33.3 |
| 6 - 10 | 9 | 25.0 |
| 11 or more | 3 | 8.3 |
| Sex worker | 2 | 5.6 |
| Average (SD) | 6.4 (6.16) | |
| **Sexual partners' characteristics (lifetime)** | | |
| HIV-positive | 19 | 57.7 |
| IDU | 8 | 22.2 |
| Male inmate | 7 | 19.4 |
| Truck driver | 5 | 13.8 |
| History of STD | 4 | 11.1 |
| MSM | 1 | 2.8 |
| **Condom use at last month with steady partner** | | |
| Always | 8 | 22.2 |
| Sometimes | 13 | 36.1 |
| Never | 15 | 41.7 |
| **Lifetime condom use with steady partner** | | |
| Always | 2 | 5.6 |
| Sometimes | 14 | 38.9 |
| Never | 20 | 55.5 |
| **Lifetime condom use with casual partner** | | |
| Always | 2 | 5.6 |
| Sometimes | 11 | 30.5 |
| Never | 10 | 27.8 |
| Had never sex with casual partner | 13 | 36.1 |
| **Substance use (lifetime)** | | |
| Had never used | 16 | 44.5 |
| Non-injection drug use | 20 | 55.5 |
| Cigarette | 18 | 50.0 |
| Alcohol | 9 | 25.0 |
| Crack cocaine | 5 | 13.8 |
| Marijuana | 3 | 8.3 |
| Cocaine | 3 | 8.3 |
| Cocaine + alcohol + cigarette | 1 | 2.8 |
| Crack cocaine + alcohol + cigarette | 1 | 2.8 |
| Crack cocaine + alcohol + marijuana + cigarette | 2 | 5.6 |
| Crack cocaine + cocaine + alcohol + marijuana + cigarette | 1 | 2.8 |
| Crack cocaine + cocaine + alcohol + cigarette | 1 | 2.8 |

IDU, injecting drug user; MSM, men who have sex with men; STD, sexually transmitted disease.

## *DISCUSSION*

In this study we found an important prevalence of HIV infection among young pregnant women living with a steady partner, with low family income, low education level, and referring early first sexual intercourse. Many reported use of illicit non-injecting drugs and unprotected sex with partners that were HIV-infected, IDU, or male inmate. These results confirm previous data reported by the Brazilian Ministry of Health and other investigations showing predominance of the heterosexual route of transmission mainly with unprotected intercourse and increased number of HIV/AIDS among younger women with low education level in other areas of Brazil, mainly in big cities.[3,4,6] In our study HIV infection was more prevalent in the age-group of 20-29 years (66.7%). Although it may reflect that these groups are the most sexually active, it may also suggest a growing epidemic. Furthermore, the earlier age of the first intercourse places young people into a group exposed to risks of unintended pregnancy and sexually transmitted diseases, including AIDS.[13]

Increased survival time of women with AIDS as well as delayed progression to AIDS during the post HAART era may result in great opportunities to become pregnant. We observed that 25% of women included in this study had their HIV diagnosis confirmed more than five years ago. Our findings showing higher pregnancy rates in HIV

positive asymptomatic women with T CD4 cell count above 350 cells/μL and low viral load compared with women with AIDS is in agreement with findings of other studies.[14] We found that 20/36 (55%) women had been pregnant before, despite being aware of their HIV positive status. In this group we found eight cases of MTCT of HIV. This cumulative rate of 40% in vertical transmission is unacceptable nowadays and news strategies for HIV prevention among young women in fertile age must be carried out. In Brazil, to protect against vertical transmission, HIV-infected pregnant women typically receive ART during pregnancy plus ZDV intrapartum and their infants receive prophylactic ZDV for 6 weeks postpartum. Furthermore, the Ministry of Health recommends that HIV-infected women in Brazil do not breastfeed their babies.[15] Considering the group of studied pregnant women in 2007, we observed that 94.4% of them had received HAART regimen in accordance with the national guidelines[15] with only one case of MTCT besides the irregular treatment adherence reported by 33.3% of treated women.

We observed that the time between diagnosis and the onset of treatment needs to be shortened. It was delayed in 66.7% of pregnant women in 2007 and almost 20% had the HIV infection diagnosed late in pregnancy, impairing or retarding adequate treatment intervention. Furthermore, it is noteworthy that only 33% of cases had a viral load below 80 copies/mL. This highlights the fact that, although free access to HIV medication is available in Brazil and extensive effortts have been deployed to foster HIV MTCT control, additional actions to improve medication adherence are needed.

Several studies have established the association between STDs and HIV infection.[16,17] Moreover, substances use also appears to have a greater effect on sexual risk.[17,18] We verified that an important percentage of women have reported drinking and smoking habits. The relationship between the use of alcohol and other drugs and sexual activity is well established. Some studies have shown that prior substances use increases the probability of an adolescent starting sexual activity.[17-19] Alcohol and cigarettes use is harmful to the health of HIV-infected people since they can inhibit the immune response and potentially decrease adherence to antiretroviral therapy.[19-23] Crack-cocaine use accelerates the progression of HIV disease.[24] In our study 57.7% of women reported that their partner were HIV-infected, 22% addicted to injecting drugs, 13.8% truck drivers and 11% had given a history of STD. Thus, our data suggest that the sexual behavior of the women's partners was the strongest predictor for HIV infection.

A pattern of heterosexual transmission and a trend towards feminization of the AIDS epidemic, which are emerging in poorly educated or unemployed women with few sexual partners during their lives, plays an important role in the epidemiological profile of HIV infection, as a result of their economic dependency of their sexual partners and the lack of power in negotiating condom use.[17,25-27] We observed that the majority of women (55.5%) have reported to have never used condoms with their steady partner. However, 58.3% reported to use condoms on an irregular basis (sometimes or never at all) when the partners were casual. The differences between the sex partners, steady or casual, regarding the lack of condom use seems to be coincident with some aspects of vulnerability to AIDS previously identified in Brazil and in other developing countries.[26,27] Another aspect to be analyzed regarding HIV transmission among Brazilian women is the increased infection rate in populations without an evident risk factor, like heterosexual women with a steady partner. Among women, strong risk factors for HIV infection were primarily related to their partners' behavior.

Our small sample size is a major drawback for the interpretation of these findings. However, as we evaluated small communities, in fact our sampling comprises almost all available pregnant women at the time when study participants were recruited. Our small sample not only represents most women living with HIV/AIDS visiting the obstetric clinic at the time of the study but almost 10% of the HIV infected female population at the region.

## CONCLUSION

This is the first report of an epidemiological evaluation of young pregnant women living with HIV/AIDS in small communities in South Brazil area where the subtype C of HIV-1 predominates. Although a clear expansion of subtype C is evident in Southern Brazil, there is no definition about possible correlation with increased risk of vertical transmission. Here, we observed that in this region of Brazil MTCT of HIV and women vulnerability to AIDS are linked with low education, poor economic conditions, early sexual contact and mainly with lack of regular condom use with the steady partner. The increase in pregnancy rates among HIV-infected women in the State of Santa Catarina, a place with predominance of HIV-1 subtype C infection, illustrates the need for continuous efforts during prenatal and neonatal care to maintain the mother's health, make changes in ART during pregnancy if necessary, and monitor the newborn's HIV status postpartum.

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