

## Prospective Study on the Prevention of Vertical Transmission of HIV in Campo Grande, Mato Grosso do Sul, Brazil, From 1996 to 2001

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This prospective study, involving 76 pregnant women infected with HIV, paired with their 79 exposed infants, was carried out between May 1996 and October 2001, at the Reference Department for Pregnant Women Infected with HIV in Campo Grande, Mato Grosso do Sul. The mean age of the pregnant women was 24 years; 88% (67/76) apparently were infected due to sexual practices; 88% (67/76) were housewives; 823% (63/76) graduated from junior high school; 14.5% (11/76) reported co-infection with Hepatitis C, 9.2% with Syphilis; 51% (39/76) learned the diagnosis during prenatal care; 67% (51/76) reported HIV clinical symptomatology and 9.2% (7/76) reported opportunistic infections. Elective cesareans were performed in 57% (43/76). The mean gestational age at delivery was 38 weeks and we found 12.5% (10/80) pronatis; 97% (74/76) had a ruptured membrane time after less than four hours and one child (1.3%) was nursed. ACTG 076 Protocol (AIDS Clinical Trial Group 076) was used in 80% (61/76) of the pregnant women, with 100% adherence; 62% (38/61) used zidovudine plus another antiretroviral in the gestation; 92% (73/79) of the infants used zidovudine after the birth and 19% (14/73) used zidovudine and lamivudine. The transmission rate in this study was 2.5%.

**Key Words:** HIV/AIDS, certical transmission, prevention/prophylaxis, Mato Grosso do Sul, Brazil.

The HIV/AIDS (Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome) epidemic is a global, dynamic and instable phenomenon, composed of several local sub epidemics. Partially mediated by social inequalities, the spread of infection with HIV/Aids has multiple dimensions and can cause significant epidemiological changes.

It is known that the vertical transmission of the HIV is the most important means of transmission for children up to 15 years old. Since the beginning of

this pandemic disease, it is estimated that 5.1 million of infants from all over the world have been infected, most of them through perinatal transmission. In 2002, over 800,000 infants were infected, 90% of them African residents [1-3].

According to the Ministry of Health in Brazil, there were an estimated 17,198 pregnant women infected with HIV in 2001, which corresponds to 0.6% of all pregnant women. One of the immediate consequences of this picture is a progressive increase in vertical transmission in our environment; 7,541 cases have been registered so far, 85.9% of which are pediatric cases recorded from 1984 to 2002 [4].

In the state of Mato Grosso do Sul, we can also see changes in the epidemic profile: An interiorization (increasing numbers of cases in rural areas) has been occurring, as well as heterosexual transmission prevalence, associated with impoverishment, and an

Received on 17 August 2004; revised 17 December 2004.

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increase in the number of cases of Aids in fertile women as well, provoking an increase in pediatric cases. In 2002, 39,657 deliveries were made all over the state; there was prenatal infection with HIV in only 60 of them, while the estimated number would be 237, based on the number of HIV pregnant women carriers, given the prevalence of 0.6% reported for our state [4].

We developed a prospective cohort study of pregnant women infected with HIV, paired with their exposed children and followed up at the Infectious and Parasitic Disease Center (CEDIP) of Campo Grande, State of Mato Grosso do Sul, between May 1996 and October 2001, to examine the prevention of vertical transmission of HIV to the infants.

## Material and Methods

The study was conducted at CEDIP between May 1996 and October 2001. CEDIP has a multidisciplinary team, which assists patients at the Service of Specialized Assistance (SSA), Day-Hospital (DH), as well as at the Therapeutic Domicile Assistance center (TDA), joining efforts for the purpose of ambulatory therapy adherence. The Protocol for a Reduction in HIV Vertical Transmission was implemented at CEDIP.

Viral load quantification, as well as CD<sub>4</sub>/CD<sub>8</sub> lymphocyte concentration exams, were requested at the first interview of the pregnant woman enrolled in the program. These were repeated at the 36<sup>th</sup> week of gestation, along with serological testing for HIV infection and Hepatitis at the state Central Laboratory of Public Health (LACEN).

### Study population

This study included 76 pregnant women who came from all over the state of Mato Grosso do Sul for a specialized follow-up after confirmation that they were infected with HIV. Among these 76 pregnant women, 80 infants were born, including four pairs of twins, and one stillborn.

### Determining the vertical transmission rate (TTV)

Possible infection of the exposed infants, whose mothers were followed up at CEDIP, or who had been diagnosed at the maternity ward, was evaluated during follow up of the newborns at our Service, up to two years of age. They were laboratory-monitored with ELISA tests (Enzyme Linked Immunosorbent Assay) every 3 months, until serum reversion and viral load was determined at 2, 4 and 8 months old.

The infants were considered infected with HIV when they had two positive viral loads after 1 and 3 months old and/or serum conversion (ELISA positive after 18 months of age, according to the Ministry of Health Guidelines) [5]. The vertical transmission rate was calculated by dividing the number of infected infants by the total number of exposed infants who were followed up.

All the infants in this study were either definitely classified as infected or had already rejected the infection.

Maternal and obstetric variables were studied, as well as variables related to infant exposure and the use of Protocol 076.

### Intervention

Protocol ACTG 076 (Aids Clinical Trial Group 076) was a multicentric random, double blind, placebo-control study carried out in 1994 to evaluate the security and efficiency of zidovudine offered to pregnant women after the 14<sup>th</sup> week, during labor, and to the newborn, for a period of 6 weeks after birth. The HIV vertical transmission rate was reduced to 67.5%. This study is known as ACTG 076 (AIDS Clinical Trials Group Protocol 076) [6].

The following abbreviations were established for the purpose of presenting the results and discussion:

*Protocol 076 Complete:* Use of antiretroviral (ARV) at the prenatal, delivery and newborn.

P - RN: use of the ARV at delivery and for the newborn.

PN - RN: use of the ARV at the prenatal and for the newborn.

P: use of the ARV only at delivery.

PN - P: use of the ARV during prenatal and at delivery.

RN: use of the ARV only for the newborn.

The intervention selected by our service was the use of the complete Protocol ACTG 076 [6], in other words, with the three components (zidovudine at gestation, delivery and for the newborn as well) or incomplete (one or two components from the Protocol) for every pregnant woman cared for at CEDIP and at the SAE of the rural areas of the state, which had led most of the pregnant women to receive assistance at the end of the gestation in our service as well to have assistance at the time of the delivery at the Campo Grande Maternities. Protocol ACTG 076, modified, was used, in other words, the use of other antiretroviral (ARV) associated with zidovudine for the pregnant women who needed a more powerful treatment due to clinical symptomatology, immunological deficiency or high maternal viral counts [7].

### Statistical Analysis

The information obtained had been stored in a computerized database using the Epi-Info 6.04b program [8] (DEAN 1997). The frequency of the several variables had been analyzed.

## **Results**

During this study 79 infants were followed up. They were born from 76 pregnant women infected with HIV who came from all over the state of Mato Grosso do Sul; four pregnant women (5.3%) had twin gestations; there was one stillborn. All of these mother-infant pairs had used the ACTG 076 Protocol complete, incomplete or modified. The temporal distribution of the diagnosed cases can be observed in Figure 1.

Figure 2 shows the age distribution of the pregnant women at the time of the delivery, which ranged from 13 to 42 years old and an average of 24 years.

Forty-four (58%) out of 76 were from the rural areas of the state and 32 (42%) were residents of Campo

Grande. When we examined other associated infirmities, we found that 25 (32.9%) reported co-infections: 11 with Hepatitis C, 5 with Syphilis, 5 with HPV (Human Papiloma Virus) and 4 with Herpes.

It was observed that 51.3% (39/76) of the pregnant women had learned their condition of being infected with HIV during prenatal care, 40.8% (31/76) had already had the diagnosis of the HIV infection previously to gestation. The six remaining (7.9%) learned of the diagnosis at the time of the delivery through the fast testing for HIV performed at the maternity.

Among the pregnant women who adhered to the study, 88.2% (67/76) were housewives, and 11.8% (10/76) were in other occupational categories, including maids, government employees and professionals, with two cases for each of these categories, while three pregnant women were employees in general services.

Regarding schooling, 31 of the pregnant women had graduated from elementary and junior high school, 26 had not graduated from junior high school, 10 graduated from senior high school, 1 did not graduate from senior high school, 2 graduated from college and 6 were illiterate.

In Table 1, we can see the epidemiological profile of the pregnant women regarding the likely risk factors associated with HIV infection.

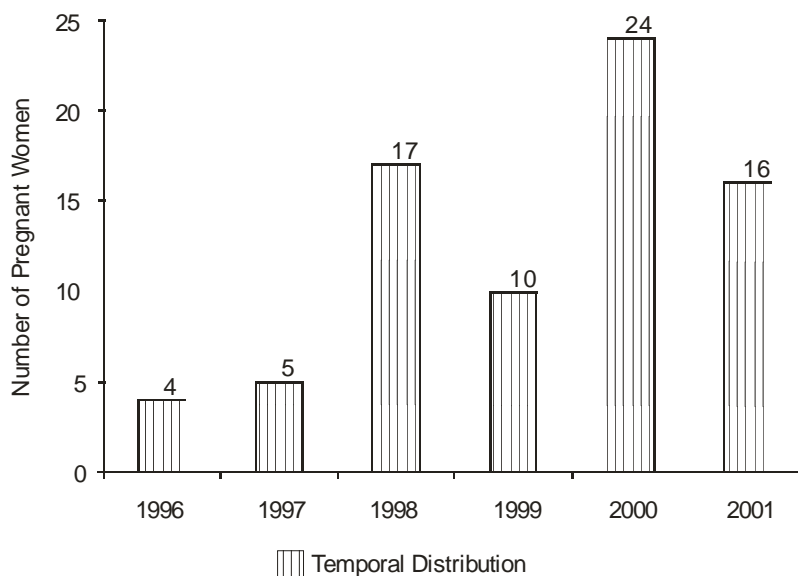
In this study, 61 pregnant women had used antiretrovirals during gestation; the largest number started at the 14th week of gestation (Figure 3).

Fifty-one (67.0%) out of 76 pregnant women reported suggestive clinical symptomatology of infection with HIV during gestation and/or delivery, and seven pregnant women (9.2%) reported opportunistic infections during gestation.

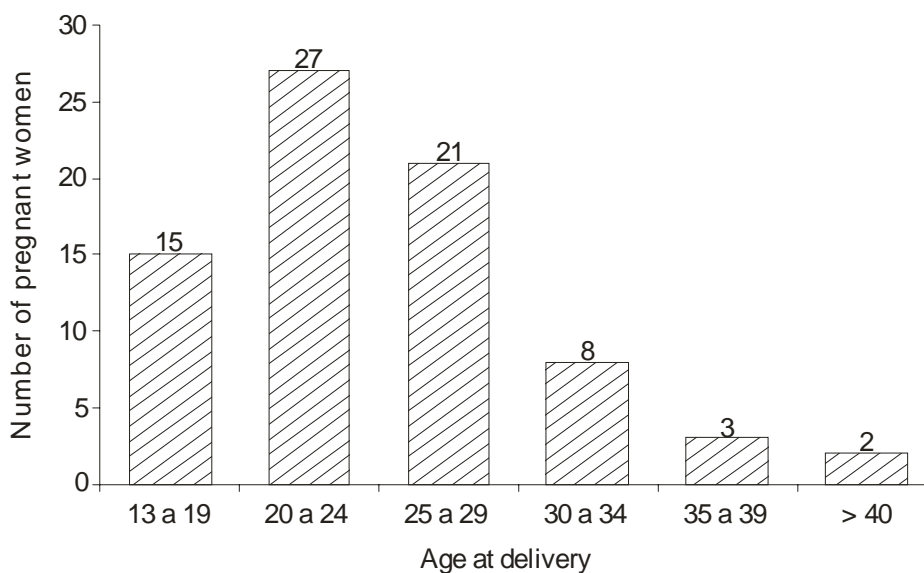
In Table 2, the viral load of 38 pregnant women infected with HIV, and using ARV, was lower at delivery; the average in these cases was 1,500 copies/mL.

Forty-three (56.6%) pregnant women were submitted to elective cesarean between the 38<sup>th</sup> and 39<sup>th</sup> weeks, 17 (22.4%) had vaginal delivery, 11 (14.5%) had cesarean delivery by obstetric recommendation. The five (6.5%) remaining pregnant women had urgent delivery, including two cases with trauma and three with prolonged labor.

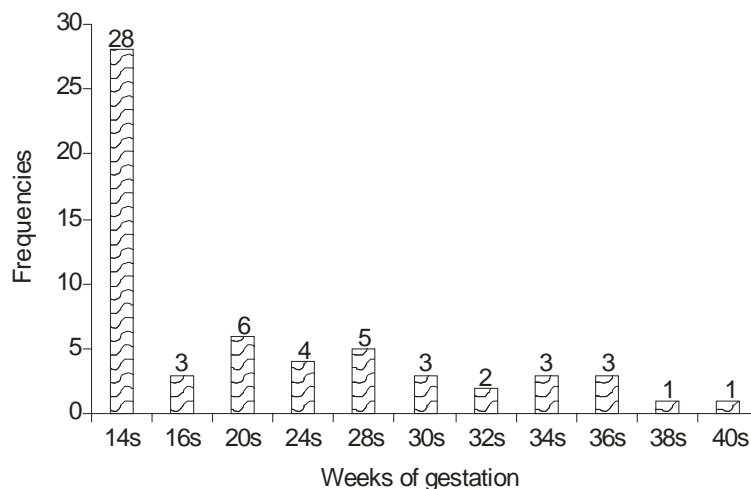
**Figure 1.** Temporal distribution of 76 pregnant women infected with HIV followed up from May 1996 to October 2001, Campo Grande, MS, Brazil



**Figure 2.** Distribution of mother’s age at delivery of 76 pregnant women infected with HIV from May 1996 to October 2001, Campo Grande, MS, Brazil



**Figure 3.** Start of antiretroviral use according to the gestational age of 61 pregnant women infected with HIV, from May 1996 to October 2001, Campo Grande, MS, Brazil



**Table 1.** Frequencies of the likely risk behaviors associated with HIV infection

Maternal Risk Behavior	N (76)	% (100)
<b>Sexual</b>		
Unique partner	36	47.4
Previous and present multipartnership	13	17.1
Partner unisexual	13	17.1
HIV-acknowledged partner	4	5.3
Partner bisexual	1	1.3
<b>Total</b>	<b>67</b>	<b>88.2</b>
Narcotic use and promiscuity	8	10.5
Narcotic drug use as an isolated factor	1	1.3
<b>Total</b>	<b>9</b>	<b>11.8</b>

**Table 2.** The viral load near delivery, of 38 pregnant women infected with HIV from May 1996 to October 2001, Campo Grande, MS, Brazil

Viral load (in copies/mL)	N	%	Accumulated %
<80	12	31.6	31.6
80 – 1,000	6	15.8	47.4
1,001 – 10,000	10	26.3	73.7
10,001 – 100,000	6	15.8	89.5
100,001 – 500,000	4	10.5	100
<b>Total</b>	<b>38</b>	<b>100</b>	

In 58 pregnant women (58.4%), delivery occurred at the 38th gestation week. We noticed that 97.4% of the pregnant women (74/76) reported membrane rupture less than four hours before delivery.

Among the 80 infants in this study, 70 (87.5%) were born at term, 10 (12.5%) were preterm, of which one was stillborn (1.25%). Among the 79 infants who were born alive, only one (1.3%) was nursed for four months. All of the 76 pregnant women of this study had used at least one of the components of Protocol 076; 58 (76.3%) pregnant women had used the three components, 15 (9.8%) had used two components and three (3.9%) only one component. The two infants who had become infected with HIV were from this latter group.

Among the 61 (80.2%) pregnant women who used ARV during prenatal, 23 (37.7%) had used only zidovudine; 29 (47.5%) had used zidovudine and lamivudine and 8 (13.1%) had used zidovudine, lamivudine and nelfinavir; one pregnant woman (1.7%) had used zidovudine, lamivudine and ritonavir.

Among the 79 infants who were born alive, 65 (82.3%) had used only zidovudine; and 14 (17.7%) had used zidovudine and lamivudine.

The average height of the infants during delivery was 47cm and 45cm for infected infants. Regarding the weight at delivery, the average of the negative infants was 2,975g and the average for the positive infants was 2,325g.

In our study, among the 79 infants, two of them reported infection with HIV, in other words, the vertical transmission rate was 2.5%.

## Discussion

Our data were similar to those of other national and international studies on the clinical-epidemiological variables that we examined. Analyzing the temporal distribution of the cases assisted at CEDIP between May 1996 and October 2001, we noticed a gradual increase in the number of children born from mothers infected with HIV, beginning in 1998. This increase in diagnosed infections with HIV in pregnant women was

expected, because, an intensive campaign was made in 1997, promoting HIV testing of all pregnant women all over the state.

Most of the pregnant women (82.9%) were between 13 and 29 years old, which is the most prevalent age of infection with HIV [9,10]; it corresponds to the fertile period of the women as well. In Mato Grosso do Sul, the cases of AIDS that are registered show a gradual increase of the epidemic among women pertaining to this age group and consequently in cases of Pediatric AIDS, unless prevention measurements are taken.

We saw 15 cases (19.8%) of youth pregnancy, as was also observed in a study carried out in Rio de Janeiro in the Total Assistance Program for HIV-positive pregnant woman [11]. Another study carried out in Manikganj, District of Bangladesh, in a High School, showed the poor knowledge level about Aids prevention among youths; 75% knew about HIV transmission through the use of injected drugs, but 90% did not trust protection with preservatives [12]. It is a fact that the number of youth pregnancies has been increasing in our country, and we should invest more in prevention programs aimed at this highly vulnerable group.

Among the 76 pregnant women, 44 (58%) came from the rural areas of the state, affirming our previous data regarding the temporal distribution of the diagnosed cases each year, which coincided with prevention actions in the rural regions, due to better adherence to the action plans of our Protocol of Assistance, by the health teams of those districts.

During the follow up, we found that 88.2% (67/76) of the pregnant women had been infected with HIV by the sexual route, which is the highest rate described for all the AIDS studies in Brazil; 47% of the cases had reported sexual exposure [13]. Among the pregnant women who had been infected by the sexual route, 36 (47.4%) indicated that they had been infected through their fixed partners, who denied the use of injected narcotic drugs or blood transfusion; but they did mention promiscuity, which is different from the data of Rio Grande do Sul, which shows a prevalence of partners who used narcotic drugs, but it is similar to findings from Rio de Janeiro [14,15] and Minas Gerais [16].

Moreover, we know that there are biological factors that support the sexual transmission of HIV from men to women (two or three times more frequently than from women to men) as well as the socio-cultural factors that prevent women from having control of their own bodies [17]. We assume that most of these women did not know that they were at risk with their partners; it reflects the little information they have concerning the risks of being infected with HIV, especially if they are involved in stable relationships [18]. As a result, most of the time, women will only look for assistance when they become sick, missing the opportunity of having timely treatment for HIV [19].

Among the pregnant women, 67 (88.2%) were housewives. Recent data shows a high prevalence of HIV in this group [18,14]. The difficulty of accepting the housewife as a vulnerable group to HIV infection has been considered as serious matter that will cause an increase in vertical transmission of HIV if prevention programs do not reach this specific group.

Regarding schooling, 63 pregnant women (82.9%) had graduated from elementary and junior high school. This data is similar to those published by the Health Ministry [20], which reported that 74% of Aids-infected individuals had up to 8 years of schooling. In Minas Gerais [16] a study in the city of Juiz de Fora, 78% had studied up to elementary and high school. Schooling was considered the main factor to explain the differences related to the risky social practices [20,21].

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