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Prevalence of HIV and *Treponema pallidum* infections in pregnant women in Campinas and their association with socio-demographic factors

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The anonymous seroprevalence of HIV and syphilis was studied by collecting umbilical cord blood samples from 5,815 women who gave birth in Campinas' hospitals throughout a six-month period. ELISA and Western blot were used for HIV, and VDRL and TPHA for *Treponema pallidum* screening. While maintaining the anonymity of the women, information was recorded on the hospital of origin, divided into university (public) and private hospitals, as well as on the form of payment (social security, private insurance or direct payment), age, marital status, education, employment and place of residence. Seroprevalence was 0.42 percent for HIV and 1.16 percent for syphilis. There was a significant correlation between a positive reaction to the two infections (p=0.02). After univariate and logistic regression analysis, only university hospitals were shown to be associated with seropositivity for HIV, whereas the same variable and an older age were associated with syphilis. All positive reactions were found either in public hospitals or among social security patients treated at private institutions. The conclusion was that HIV infection is becoming almost as prevalent as syphilis among this population, and affects primarily the lower socio-economic strata. This suggests that routine, voluntary HIV serology should be considered and discussed with patients during prenatal or delivery care whenever a population shows a seroprevalence close to or greater than 1 percent.

UNITERMS: Human immunodeficiency virus. HIV, prevalence women, gestation. Umbilical cord blood.

INTRODUCTION

By mid-1991, a total of 371,802 AIDS cases had been reported worldwide; 18,113 of these were in Brazil, which ranked third in number of cases.⁵² The spread of the epidemic has been very rapid throughout the world, but has not followed the same model in every country. The identification of several epidemiologic

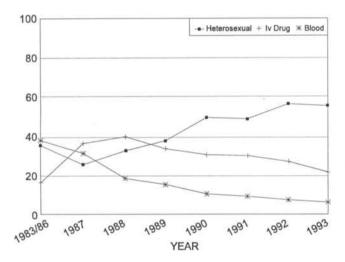
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Eliana Amaral Divisão de Obstetrícia do CAISM - UNICAMP Rua Alexander Fleming, 101 Campinas/SP - Brasil - CEP 13081-970 patterns has contributed to a better understanding of women's participation in the spread of the disease.

Epidemiologic pattern Type I, found in the United States and in some areas in Latin American, corresponds to populations in which homosexual men are the most affected group, followed by intravenous drug users and a small number of women. Type II pattern is found in Africa and the Caribbean, with predominantly heterosexual dissemination and no difference in prevalence between men and women. Pattern III refers to countries with low AIDS prevalence even among groups considered high risk. Such patterns, however, can change with time, giving rise to an intermediary pattern Type I/II, found in regions where initial dissemination was among homosexuals and drug users, but where the incidence of

the disease has been expanding through heterosexual transmission.⁴¹ The World Health Organization considers Latin America, including Brazil, to be part of this intermediate group.^{36, 39}

According to information from the Brazilian Ministry of Health, the first male AIDS case in Brazil was reported in 1980, but the first female case was not reported until 1983. In 1984, there was one infected woman for every 124 men, but in 1993 the ratio was 1:4. The evolution of AIDS distribution among Brazilian women has shown a decrease in infection through blood and blood products, but a progressive increase in infection by heterosexual contact, which today is the main mechanism for the transmission of HIV infection (Fig. 1).



The immediate consequence of the higher prevalence among women is the vertical transmission of the infection to their children in a proportion that varies from 12.9 to 39 percent. 9.24,25,45,49 In Brazil, during the first half of 1993, vertical transmission represented 87.9 percent of all pediatric AIDS cases, whereas up to 1986, 78 percent of HIV infections among children had been acquired through blood. 12

Knowledge about the dimension of the epidemic is required to educate the population to adopt preventive measures, and provides the basis for sensitizing those who are politically responsible to make decisions which support control programs. This knowledge is also required for the evaluation of the impact caused by control measures. The indicator commonly used to assess the dimensions of the epidemic is the number of AIDS cases reported to health authorities. Nevertheless, such methodology affords only a late insight into the dynamics of the infection, as the numbers obtained refer to individuals who had been contaminated several years earlier.⁶

Prevalence studies of HIV infection constitute a more efficient method to evaluate the dimension of the epidemic and to follow its dynamics, providing global and updated information on contamination levels, which can then be applied to several population groups. ^{6,48} Their repetition in relatively stable population groups through so-called "sentinel surveillance," provides a long-term view of the evolution of the epidemic. The multiplication of these "sentinel surveillance" studies permits efficient, swift and economical screening, as well as a monitoring of the infection. ^{20,47}

The prevalence of the infection among women may be a good indication of the situation among the general population when non-selected groups are evaluated. The most comprehensive and practical way to reach unselected women is to perform serologic tests on patients attending prenatal clinics or at birth. ^{29,33,38}

Another reason for investigating the prevalence among delivering women is the risk of contamination for health professionals. ^{15,16} Prospective studies of the risk faced by health professionals exposed to seropositive blood has shown a 0.3 percent rate of seroconversion after accidents with contaminated needles or cutting instruments, and no seroconversion after exposure of the mucosa. ³⁰

The professional assisting at a birth is exposed to much larger quantities of blood and other body fluids than most surgeons in non-obstetric procedures. Therefore, prevalence data on syphilis and HIV among pregnant women is also useful to highlight the need to take preventive measures. This applies to hospital management, to ensure the adequate provision of equipment, and to doctors and nurses, so as to educate them to take protective measures.

In Brazil, the medical literature shows a prevalence ranging from 1.0 percent to 3.75 percent in prenatal patients/delivering women in specific population groups,

Table 1
Proportion of valid samples to total births by hospital

Hospitals	Samples n	Deliveries N	n/N %
1	759	1,740	66.58
2	1,380	1,602	86.14
3	1,186	1,526	77.72
4	725	794	91.31
5	1,765	4,608	38.30
Total	5,815	9,670	60.13

selected from where there is a high concentration of women presenting high-risk behavior for HIV infection. 19,23,43 At CAISM, the Women's Hospital of the State University of Campinas (UNICAMP), HIV infection was diagnosed during pregnancy in 0.47 percent of women delivering between September 1988 and December 1990. However, the actual prevalence was unknown, as serologic tests were performed only on women with known risk factors for HIV infection.²

Routine testing creates other problems, as the worldwide ethical norm for HIV infection screening establishes that the individuals to be tested should give their informed consent whenever identified by the person requesting the test. 1,14,18 Prevalence studies with identified subjects who agree to be tested lead to a underestimation of up to 50 percent, as a consequence of the selfexclusion of individuals at higher risk. 22.30.31.50 The recommended ethical procedure for conducting random seroprevalence studies is to carry out anonymous serology, both on the part of the individual being tested and on the part the researcher, in a double-blind study.3.6.47.48 This study design is considered ethical, because the blood sample becomes the object of the study, as the identity of the patients is unknown. This methodology has already been used in several countries, 27.30,33,50 and is recommended by international organizations dealing with AIDS control after careful consideration of its advantages and disadvantages. 38,47,48

The main advantage of this method is that it provides a more accurate evaluation of prevalence. At a time when few physicians pay proper attention to HIV infection, we judged raising awareness on the actual prevalence to be a priority that requires the adherence to methodology internationally recommended for this purpose.

The development of this study in Campinas was justified because the city was ranked ninth in absolute numbers and seventeenth in AIDS incidence coefficient, 12 which placed the city in an intermediate situation among Brazilian urban centers. A parallel study on *T. pallidum* infection was added with the goal of comparing the prevalence of the two diseases, considering also that syphilis serology is part of the standard prenatal routine recommended by the Ministry of Health. 10 This has the additional purpose of studying lues seropositivity as a risk factor for HIV infection.

SUBJECTS AND METHOD

A cross-sectional study was carried out between April 1 and September 30, 1991. Umbilical cord blood samples

were collected in all deliveries occurring at the five hospitals registering the highest number of obstetric cases in Campinas (83 percent of deliveries). Three of the maternity hospitals are part of private or philanthropic organizations, and the other two are university hospitals, which make up part of SUS (Public Health System). Samples were collected during all births, without any selection criteria. Therefore, all types of patients were included, from those whose expenses were covered by SUS to those who had private health insurance or paid directly. The clinical boards of directors and the hospitals' ethics committees approved the development of the study after evaluating the proposal.

Umbilical cord blood samples (10ml) were collected without the addition of any anticoagulant, in all births, independent of the form of delivery (vaginal or by Caesarean section). The patients' initials, date and time of delivery were written on adhesive labels, with specific serial numbers for each hospital printed on the same label. Samples identified only by the label were collected daily by a research assistant from the five hospitals and delivered for serologic testing to the Hemocentro - Campinas, located at the State University of Campinas (UNICAMP).

An ELISA test (Abbot HIV 1 EIA, manufactured by Abbott Laboratories in Brazil) was carried out on each sample, followed by Western blot (Du Pont) whenever ELISA results were positive or inconclusive. Western blot was considered positive when positive results were found for bands p 24, p 31, gp 41 or gp 120/gp 160, according to Biotech du Pont, criteria corroborated by the U.S. Food and Drug Administration. To Screening for T. pallidum infection was conducted by VDRL quantitative test (Boehring), and all positive samples were tested for confirmation by TPHA (Biolab).

In the meantime, research assistants collected epidemiologic data from hospital records, removing any personal identification which could tie serology results to specific patients. To protect anonymity, only numerical identification was kept.

Dependent variables studied were: HIV infection and *T. pallidum* infection. Independent variables studied were: type of hospital (university or other); mode of payment for hospital bill (meaning how hospital and medical costs were covered); age; marital status; education; professional occupation; and city of residence.

All information was recorded on a special form. All forms without the serology results were excluded from the analysis. When serology results did not have the corresponding form with information on the independent variables, they were used only to estimate the general prevalence of the two infections (113 cases). Results of

Table 2 Number of blood samples lost to analysis, by reason

Reason	ELISA	VDRL
- hemolysis	693	693
- insufficient material	15	15
- plasma formation	0	19
- broken vessel	6	6
Total samples lost	714	733
Valid samples	5,101	5,082
Total samples collected	5,815	5,815

serological tests were entered into a IBM-PC computer using the DBase III Plus program; statistical analysis was carried out on the SPSS-PC program. Univariate analysis was concluded using dichotomized variables through the Q-square test and, when necessary, through the Yates and Fisher correction procedures. Multiple analysis was carried out using the logistic regression technique.

RESULTS

During the period of sample collection there were 9,209 births. However, because of failures in sample collection, only 5,815 blood samples were obtained, corresponding to 60.13 percent of all deliveries. The number of births, samples collected, and resulting proportion by hospital are shown in Table 1.

More than 10 percent (714) of the samples were rejected for different reasons. Spontaneous formation of plasma in place of serum rendered 19 samples adequate for HIV serology, but not for *T. pallidum*. Consequently, 5,101 valid samples were selected for the ELISA test and 5,082 for the VDRL test (Table 2).

Table 3
Seroprevalence for HIV and *T. pallidum* by hospital

Hospitals	HIV n (%)	T. pallidum n (%)	Ratio HIV/ T. pallidum
1	4 (0.6)	13 (1.9)	1:3
2	12 (1.0)	24 (2.0)	1:2
3	3 (0.3)	9 (0.9)	1:3
4	0 (0.0)	3 (0.5)	-
5	2 (0.1)	10 (0.7)	1:5
Total	21 (0.4)	59 (1.2)	1:3

Table 4
Correlation between seropositivity for HIV and *T. pallidum*

HIV		T. pallidum	
	Positive	Negative	Total
Positive	2 (30%)	18 (0.4%)	20
Negative	57	5,004	5,061
Total	59	5,022	5,081

p = 0.02 (Fisher's test)

Twenty-two positive and five inconclusive results were found by the ELISA method for HIV. Twenty positive and one inconclusive ELISA-samples were confirmed as positive by the Western blot test. In the non-specific test for *T. pallidum*, 61 reacting samples were found, with quantitative VDRL less than or equal to one-eight. The specific proof confirmed the positivity of 59 samples, with evidence that the remaining two were false-positive.

Thus, the HIV seroprevalence found in the total collection of samples was 0.4 percent or 4 per 1000, varying from 0 percent to 1.0 percent among participating hospitals. General seroprevalence for *T. pallidum* was 1.2 percent, varying from 0.5 percent to 2.0 percent. The highest prevalence was observed in university hospitals, and no HIV infection was detected at the one hospital which attends only private patients and those with private health insurance (Table 3).

There was a significant correlation (p<0.02) between seropositivity for syphilis and HIV. HIV infection prevalence was seven times higher in positive *T. pallidum* samples (3.0 percent), than in the negative *T. pallidum* group (0.4 percent) (Table 4). The univariate analysis showed a correlation of both infections with university hospital and SUS payment mode; there also was a correlation with age over 24 for *T. pallidum*, and with the absence of a marital union for HIV (Table 5). No HIV seropositive samples were found among private patients or those who had private health insurance; the 21 seropositive samples were found among patients using SUS. Multiple regression showed, for both infections, a correlation with university hospital care and, for syphilis only, a correlation with older age (Table 6).

DISCUSSION

The 0.4 percent HIV seroprevalence found among childbearing women in Campinas can be considered low,

Table 5
Summary of univariate analysis according to variable category

		HIV		T. pallidum	
Variables	Categories	Prevl. (%)	р	Prevl. (%)	р
Type of Hospital	University Other	0.8 0.2	0.0001	2.0 7.0	0.0001
Mode of Payment	SUS Other	0.6 0.0	0.006	1.6 0.3	0.0005
Age	≤ 24 ≥ 25	0.4 0.4	0.831	0.9 1.5	0.045
Marital Status	In union Other	0.3 0.8	0.037	1.1 1.6	0.244
Education in Years	4 or less 5 or more	0.3 0.5	0.589	1.4 0.9	0.148
Occupation	Yes No	0.3 0.5	0.534	1.1 1.3	0.499
Residence	Campinas Other	0.4 0.3	0.879	1.2	0.803

Prevl. = Prevalence

while 1.2 percent for *T. pallidum* is classified as intermediate.⁵¹ The study has shown, however, great inequality in the distribution of cases; HIV and *T. pallidum* prevalence in university hospitals was twice as high as in the total of the samples (close to 1 and 2 percent, respectively). This classified them as having intermediate to high rates of these infections. The same ratio of one HIV to three *T. pallidum* infections was observed, with minor variations, in each hospital and in the entire collection of samples.

The evaluation of the prevalence found in this study should take into consideration that the precision of umbilical cord blood screening in the assessment of maternal serologic condition is questionable. Its accuracy for HIV infection has not yet been studied. As for syphilis, RAWSTROM and BROMBERG44 compared serology in maternal, umbilical cord and neonate blood, using the rapid plasma reagent (RPR). These authors found 33 percent of false-negative results in cord blood compared to maternal infection. On the other hand, 2 percent of the cord blood samples were positive while the maternal samples were negative. The same proportion of false-negative results for syphilis, in cord blood, had been found by MILLER et al.37 If the same margin of error were valid for HIV, the real maternal prevalence in our sample would be 0.6 and 1.8 percent for HIV and T. pallidum, respectively.

These results are in agreement with other evidence of increased HIV infection rates among Brazilian women of reproductive age, such as the increasing male/female ratio in the number of AIDS cases reported to the Ministry of Health, 12 and the growing infection rates among the women delivering at the university hospital in Ribeirão Preto. 23

A prevalence of 0.4 to 0.6 percent in Campinas, and of 1.0 to 1.5 (if cord blood testing detects only two-thirds of maternal infections) in university hospitals should call the attention of medical authorities to the need for HIV screening in pregnant women.

The cost of HIV serology has limited the use of testing during prenatal care in Campinas. Only one university hospital offered this test, but restricted it to pregnant women who referred risk factors for HIV contamination. In view of the results of this study, this attitude may be too passive considering the expansion of the epidemic in the city.

The U.S. Public Health Department, in 1987, and the American College of

Obstetricians and Gynecologists, in 1988, recommended that counseling and serologic tests should be offered in all centers assisting high-risk women or groups with increasing seroprevalence. In New Jersey, a HIV prevalence rate of 4.9/1000 in umbilical cord blood samples (similar to what was found in Campinas) was the justification for offering voluntary HIV testing to all childbearing women and those intending to become pregnant. 27

The advantage of routine prenatal screening for HIV is that pre- and posttest counseling may provide opportunities for adequate information/education and dialogue leading to genuine behavior modification. Despite the strong emotional impact of the infection diagnosis during pregnancy, there is a benefit in the closer clinical surveillance of the infected pregnant woman and her newborn, which seems to improve the prognosis for seropositive patients.¹³

The similarities of HIV and *T. pallidum* infections in young women, allied to their close prevalence, suggests the need to treat them in a similar way at the programmatic

Table 6
Value for factors associated with HIV and *T. pallidum* in multiple logistic regression

Factors	HIV	T. pallidum
University Hospital	0.0064	< 0.0001
Older Age	N.S.	0.0115

level. For example, the populations at risk and the educational activities to prevent the two infections frequently overlap. The crucial difference is that HIV infection is non-treatable and carries a strong stigma, which justifies the requirement of informed consent prior to HIV testing, while serologic diagnosis of syphilis is routinely done without ethical conflicts.

In light of our results and the above considerations, it is suggested that HIV testing should be included in routine prenatal care in Campinas, as well as in all regions where infection rates have reached intermediate or high levels, such as Santos, Ribeirão Preto, São Paulo and Rio de Janeiro. ^{21,23,26,46}

Studies of pregnant women in the United States have shown that acceptance of HIV testing during the prenatal period reaches only 76 percent, 4.5 and that infected women are more common among those who refuse to be screened for HIV.35

The alternative approach, selectively screening women with risk factors for HIV infection, becomes less efficient, because the higher the prevalence of HIV among the general female population, the higher the proportion of infected women not detected by risk behavior screening. ^{22,34,50} Thus, the clinical-epidemiologic evaluation of risk factors has not been effective in identifying all infected women, leaving 50 - 66 percent of positive cases undiagnosed. ^{23,28} Therefore, several authors conclude that with prevalence reaching significant levels, routine and universal consented prenatal testing is recommended. ⁴⁸

The need and convenience of adopting this strategy depends on periodic reevaluation. The intermediate position of Campinas in the scenario of the epidemic and its populational characteristics suggest that it may serve as a sentinel city for national surveillance of the disease. To this end, repeated prevalence studies among childbearing women should be carried out in Campinas at regular intervals.

The problem is that prevalence studies must be blind and universal to be accurate. The ethics of carrying out blind testing for HIV infection has been questioned because it means not identifying HIV positive women who will deliver and breastfeed their babies without being informed of their condition, or of the precautions they should take with their sexual partner and the newborn. The available alternative should be considered for ethical judgement.

The present situation in Campinas, as well as in the overwhelming majority of births in Brazil, is that women are not given the option of HIV testing. The limiting factors are the lack of available laboratory facilities, the cost of

the kits for ELISA and, particularly, of the Western Blot test. As described above, at the time the present study was carried out, only the laboratory of one of the university hospitals was agreeing to do the ELISA test for a selected group of high-risk women attending a prenatal clinic, whereas women delivering in the other hospitals in the city did not have access to HIV testing.

If HIV screening had been available for all patients delivering in Campinas at the time of the study, it would have been unethical to interrupt their routine for research purposes. This was not the case, as no routine was altered during the study period. Still, it could be criticized from an ethical point of view, that as the HIV test had been administered, even throughout a short period, those women and their families could have benefited from information about their condition. This would have required identifying the samples with the name of each woman. For this, we would have had to request the patients' consent, according to accepted ethical principles. Previous experience shows that about 25 percent of the women would not have consented, and that the prevalence of HIV infection is higher exactly in this group. 21,28,31,50 Thus, if we had followed the first procedure we would have failed to accomplish the purpose of the study, namely, to evaluate the real prevalence of HIV infection among women giving birth in Campinas, as those with the highest prevalence might not have been tested.

The ethics of blind surveillance testing has been the subject of profound discussions by working groups in Europe, the United States, Canada and the World Health Organization. An American Journal of Public Health editorial recently concluded that "seroprevalence studies are not only ethically permissible, but their conduct is an ethical resposibility for those responsible for public health". This opinion was endorsed by an editor of Bioetica (a journal published by the Brazilian Federal Council of Medicine), who reviewed the article mentioned above. 8

Another problem with blind, anonymous serology is that it does not permit the detailed study of sociodemographic factors potentially associated with these infections. Even considering such methodologic restrictions, the present data suggest that there is a link between socio-economic situation and infection, both for HIV and *T. pallidum*, as all the positive cases were women treated by SUS; none of them were private patients or women with private health insurance. The correlation between HIV infection and poverty has been described by several authors.^{32,42} In the United States, this connection is indirectly observed in the disproportionate prevalence of the infection among blacks and Hispanics.

Consequently, it appears that HIV infection is another example of the social disadvantage of the poor. The current difficult situation of the public health system in Brazil can not be an excuse to ignore the progressive contamination of the population with HIV. In 1988, the Ministry of Health (MOH) rejected a proposal for universal testing for HIV during prenatal care. Since then, the MOH has not made a

single statement concerning this issue. ¹¹ Any change in policy should be based on current data on HIV prevalence, such as that provided by this study. We hope that our results may help many women in the future if these results, and those of a later second round, are successful in convincing health authorities of the need for routine HIV screening during prenatal care.

RESUMO

Estudou-se soroprevalência anônima para Vírus de Imunodeficiência Humana (HIV) e sífilis através de coleta de sangue de cordão umbilical de 5.815 parturientes, em hospitais de Campinas, SP, por um período de seis meses. Foram utilizados testes de ELISA e "Western blot" para diagnóstico de infecção pelo HIV, e VDRL e TPHA para *Treponema pallidum*. Mantendo-se o anonimato, colheram-se informações sobre hospital de origem, dividido em universitário (público) e privado, forma de pagamento (seguro social, seguro particular e pagamento direto), idade, situação marital, escolaridade, ocupação e cidade de procedência. A soroprevalência para HIV foi 0,42 percent e para sífilis foi 1,16 percent. Foi encontrada associação entre ambas, isto é, maior prevalência da primeira nas amostras positivas para lues (p=0,02). Após análise por regressão logística, apenas o hospital universitário mostrou-se associado à soropositividade para HIV, e a mesma variável e maiores idades se relacionaram à sífilis. Todas as reações positivas para HIV foram encontradas em hospitais universitários ou em pacientes cujos partos foram pagos pelo SUS em hospitais privados. Concluiu-se que a prevalência de infecção pelo HIV está se aproximando daquela encontrada através de sorologia para sífilis, afetando pacientes de camadas socioeconômicas menos favorecidas. Sugere-se considerar a indicação de sorologia rotineira e consentida para HIV no pré-natal, quando a população mostrar prevalência de infecção próxima ou maior que 1 percent.

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