

Vertical Transmission of Human T-Cell Lymphotropic Virus Type 1: Impact of Counseling Seropositive Women

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Abstract

Objective: Although HTLV-1 is associated with severe diseases, there is ongoing vertical transmission since prenatal HTLV screening is not implemented in countries where the virus is present. We performed a cross-sectional analysis to verify the impact of counseling pregnant HTLV-1 seropositive women, who participate in the GIPH cohort study in Brazil, on this vertical transmission.

Methods: GIPH study started in 1997 as an open prevalent cohort of HTLV-positive individuals. Children born from HTLV-1 seropositive women were divided into: (1) born before and (2) after the participation of mothers in the GIPH cohort ("GIPH babies"). The pregnant women participating in the study were counseled in order to prevent viral transmission, with recommendations of avoiding breastfeeding, giving infant formula, and preferably having the delivery by cesarean section.

Results: We identified 54 children born of HTLV seropositive mothers. 3/21 (14.3%) of the children born from mothers who received no counseling were found positive for HTLV-1, in contrast to 1/18 (5.6%) of the "GIPH babies", whose mothers received counseling. 15 children were not tested, either due to the family's refusal or impossibility to locate them.

Discussion: We found that it was worthwhile to counsel the mothers, since, as previously reported in the literature, we could observe a decline in the vertical transmission, which demonstrates the importance of prenatal screening of the virus. These actions should be widespread in countries where HTLV is present, in order to avoid the silent transmission of HTLV and future diseases in children born from positive mothers.

Keywords: HTLV-1; Vertical transmission; Breast feeding; Counseling; Brazil

Introduction

HTLV-1 is endemic in Japan, the Caribbean, Africa, South America and the islands of Melanesia. It is also present in The United States and Europe, where it is tested in blood banks [1]. In Brazil, Argentina, Colombia, Peru and Caribbean countries such as Guadeloupe, Jamaica, Martinique, and Trinidad and Tobago, seroprevalence rates range from 1 to 10% [2]. However, these figures may be as high as 37%, as reported in selected populations in Southwestern Japan [3,4].

The clinical manifestations associated with HTLV-1 can be divided into three categories: neoplastic, inflammatory and infectious. The diseases classically described in association with this virus are Adult T-cell Leukemia (ATL), HTLV-associated myelopathy/Tropical Spastic Paraparesis (HAM/TSP) and uveitis, as well as infective dermatitis, strongiloidiasis and multiple skin and autoimmune disorders [5].

The most important routes of HTLV-1 transmission occur through sexual intercourse (woman-man or man-woman), blood dissemination (injectable drugs or blood transfusion), and vertically (from mother to child) mainly by breastfeeding [6]. Transmission

efficiency through the mother to child route is estimated to be more than 20% and has been correlated with individual variables, such as the proviral load of HTLV-1, HLA type, as well as duration of breastfeeding [7]. Transmission from mother to child during the intrauterine or peripartum period has been reported to occur in less than 5% of cases [2].

Vertical transmission of HTLV-1 may include three routes: intrauterine, during childbirth, or postnatal. Intrauterine transmission has been analyzed by a study with MT-2 cells, in which a human T cell line that produces HTLV-1 was injected into pregnant rats, resulting in detection of HTLV-1 provirus by PCR in fetal liver and spleen [8]. During childbirth the direct transfer of body fluids and cells from mother to child must be considered.

The postnatal mother to child infection occurs through breastfeeding [9]. Breastfeeding is generally regarded as a risk factor for HTLV infection in exposure periods longer than 6 months, which increases with high maternal proviral loads [10,11].

Intrauterine or peripartum maternal-infant transmission seems to be less important and can be prevented by placental cell apoptosis induced by anti-HTLV-1 antibodies [12].

The development of specific diseases associated with HTLV-1 is apparently related to the infection route. ATL development has been associated with breastfeeding [13]. Approximately 1-5% of children infected through vertical transmission will develop ATL at some point in their lives [6]. On the other hand, HAM/TSP has been associated with HTLV-1 transmitted through blood transfusion. Cases of ATL associated with post-transfusional HTLV-1 infection are exceptional [14].

Counseling the HTLV-1 seropositive patient will depend on the situation in which the diagnosis is performed. In Brazil, this counseling is mainly conducted at blood transfusion services, due to mandatory serological screening for HTLV since 1993. Counseling of HTLV-positive pregnant women includes recommendations of not breastfeeding, not donating breast milk, and cesarean delivery, although the latter is controversial [6].

In Japan, HTLV-1 screening in prenatal care, followed by counseling positive women to avoid breastfeeding, led to a significant reduction in infection rates between naturally breast fed and artificially breastfed children [14].

In order to assess the rate of vertical transmission in the State of Minas Gerais, Brazil, Ribeiro et al. [15] analyzed 55,293 blood samples from newborns and found 52 (9.4/10,000) reactive samples in the HTLV-1 Elisa screening test. 42 of the mothers of these children with reactive blood (7.6/10,000) were confirmed positive for HTLV [15]. This strategy allowed the evaluation of HTLV-1 infection in a large population.

The present study evaluates the effectiveness of counseling seropositive women on vertical HTLV-1 transmission, in a long-term cohort study.

Methods

Study design and data collection

This was a cross-sectional study inserted in the ongoing cohort of the Interdisciplinary HTLV Research Group (GIPH). The GIPH prospective study congregates seven institutions and has been going on for 18 years, monitoring seropositive and sero indeterminate HTLV individuals, mainly former blood donors of the public blood center (Hemominas) as well as their families and sexual partners. We called "former blood donors" those individuals who were blood donors until they were found to be positive to a pathogen screened at the blood center. The blood donor candidates were either donating for the first time and found to be positive to HTLV and therefore could not donate again (and their blood was discarded), or were already repeat donors who sero converted to HTLV and were excluded from the donor pool.

Patients with HAM/TSP from a rehabilitation hospital also participate in the GIPH study. For the present study, we evaluated between March 1997 and April 2013 the children of HTLV-1 positive

women, who were pregnant during the study and/or had children previously to entering the cohort.

HTLV-1 testing

Laboratorial diagnosis of HTLV-1 was reached when a sample was repeatedly reactive in the screening test (ELISA, Ortho Clinical Diagnostics, Rochester, NY, USA) and confirmed by a positive Western Blot (GLD HTLV Blot 2.4, Gene labs Diagnostics, Singapore).

Database structure and statistical analysis

For the present study we used the cohort database, and statistical analysis was performed using EpiInfo® software.

Ethical aspects

This study was approved by the GIPH Study and by the Hemominas Ethics Committee (CEP).

Results

We identified 54 children born from HTLV-1 seropositive women in the GIPH cohort. We tested 39 of these for the virus. 21/39 (53.8%) were born prior to the study and the mothers did not receive counseling (Figure 1).

18/39 (46.2%) were born after the GIPH study began and their mothers received counseling; these were referred to as "GIPH babies". 3/21 (14.3%) of the children born from mothers who received no counseling were found positive for HTLV-1, two females and one male. In contrast, only one of 18 (5.6%) of the "GIPH babies", whose mothers were counseled, was positive. She was a female. Fisher's exact test showed no statistical significance between groups ($p > 0.05$).

The three children who were found positive to HTLV-1 (3/21) were breast fed for more than four months. Two of them were born vaginally, and one was born by cesarean section. None of them received blood transfusion. The age of the three patients (two females and one male) tested before the mother's participation in the cohort was over 25 years old, thereby they were already sexually active and their sexual partners were negative.

The only HTLV-1 positive child (1/18) of the group of mothers who received counseling has possibly been breast fed for more than three months by her mother. This mother showed much resistance to not breast feeding her child, and we have all reasons to believe that despite the counseling, she did breastfeed the baby. This child was born by cesarean section, was never submitted to blood transfusion, and had not another risky situation to acquire the infection.

Fifteen children could not be tested, either due to refusal of the mother or to the impossibility to locate them due to change of address and consequent loss of follow-up.

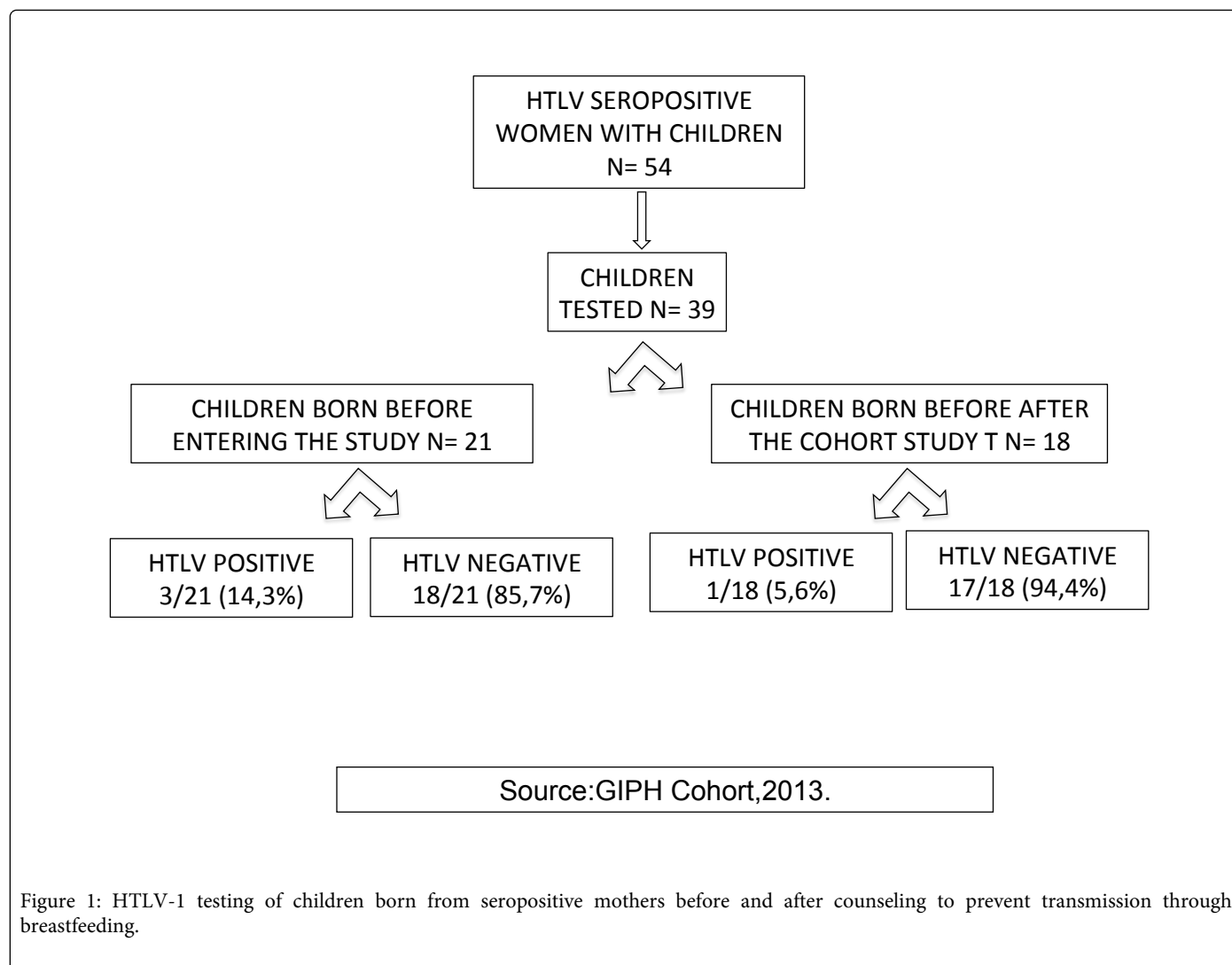


Figure 1: HTLV-1 testing of children born from seropositive mothers before and after counseling to prevent transmission through breastfeeding.

Discussion

Of the 54 children born from HTLV-1 seropositive women in our cohort study, we were able to test only 39. We observed a smaller proportion of transmission among the children whose mothers were advised not to breastfeed and to give the infant formula instead, as previously reported in literature, especially in Japan [9]. Although our numbers were not large, there was a predominance of females, which coincides with prior reports [16].

We observed a high number of refusals to test the children, as well as those who were impossible to locate. The resistance to test for HTLV-1 was also observed in the cohort regarding testing of spouses or sexual partners. This could be due to a fear of being rejected, as well as the feeling of guilt and denial of possible vertical or horizontal (sexual) transmission. Moreover, there are socioeconomic barriers, for this infection occurs in individuals who are usually in a less privileged social situation and have reported limitations in resources to access public transportation.

One of the reasons for not being able to trace many of the children is that the families frequently change their addresses and are therefore lost to follow-up. In our cohort, we observed that participants usually do not maintain contact and provide new addresses and phone

numbers as requested, unless they develop some symptom or disease that might be related to HTLV. Being asymptomatic, the mother might not see the significance in testing and prevention, and consequently loses the opportunity to avoid vertical transmission and dissemination of the virus.

Due to the lack of vaccines for HTLV, prevention must be achieved through the detection and counseling of infected individuals. Therefore, it is of utmost importance to detect seropositive women in the prenatal care setting and counsel them not to breast feed, as this is the main route of HTLV vertical transmission.

It is possible to avoid vertical transmission even if the seropositive mother is detected indirectly through neonatal screening, a strategy used by Ribeiro et al. [15]. These authors identified passive maternal IgG against HTLV in the neonate, allowing an early intervention that is ideal since the duration of breastfeeding is one of the factors associated with mother to child transmission of HTLV. Studies in Japan have demonstrated that children breast fed for a period superior to six months have higher chances of HTLV transmission (20-30%) [6,9].

In the case of milk banks, we recommend testing for HTLV-1 before the donation even if the milk is subjected to viral inactivation procedures, such as pasteurization [17].

Another important point is to define the indications for cesarean delivery in HTLV-1 seropositive pregnant women, in order to avoid unnecessary interventions without the concrete benefit of reducing viral transmission to the child.

In underdeveloped and developing countries, due to risk of malnutrition, it is vital to ensure alternative feeding for the newborn.

Although the results presented here are preliminary, there was a smaller proportion of transmission in children whose mothers were counseled. Further studies with an increased number of participants will be able to better establish the impact of counseling on vertical transmission in the GIPH cohort. The data and arguments addressed in this study have contributed towards the implementation of HTLV-1 testing for at-risk pregnant women by the City of Belo Horizonte, Minas Gerais, Brazil, which will also offer six months of infant formula for children born from seropositive mothers. This shows the importance of not only acquiring knowledge on the pathogens circulating in a certain area, but also of articulating research with public policies in order to reduce transmission, and therefore disease, in populations.

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