



# Complying with the HIV test algorithm for diagnosing children aged from 1 to 18 months born to HIV-positive mothers

## Cumprimento do algoritmo para o diagnóstico do HIV em crianças de 1 a 18 meses nascidas de mães HIV positivas

RIALA6/1738

Marcella Kelyva PIERRE, Denise Maria Bussoni BERTOLLO, Juliana Kindler FIGUEIREDO, Márcia Maria Costa Nunes SOARES\*

\*Correspondence to: Laboratório de Biologia Molecular, Núcleo de Ciências Biomédicas, Centro de Laboratório Regional Instituto Adolfo Lutz São José do Rio Preto – X, Rua Alberto Sufredini Bertoni, 2325, Maceno, São José do Rio Preto, SP, Brasil, CEP: 15060-020. Tel: 17 3224 2602, ramal 707. E-mail: [marcia.soares@ial.sp.gov.br](mailto:marcia.soares@ial.sp.gov.br)

Recebido: 10.04.2017 - Aceito para publicação: 08.05.2018

### ABSTRACT

The evolution of the epidemic of HIV in Brazil has especially affected women, and the control of mother-to-child transmission of HIV (MTCT) has been a new challenge to be faced. This study assessed the compliance with the algorithm recommended by the Ministry of Health (MH) for diagnosing the children born to HIV-positive mothers, followed-up in the Regional Central Laboratory of the Instituto Adolfo Lutz of São José do Rio Preto-X, and to evaluate the occurrence of mother-to-child transmission. This cross-sectional descriptive study collected data on the CD4<sup>+</sup> T-cell count and viral load System for Controlling Laboratory Examinations (SISCEL) and System for Hospital Management (SIGH) from January 2009 to December 2014. In this period, 265 children were registered, being 141 (53.2%) male and 124 (46.8%) female; and only 217 (81.9%) complied with the algorithm recommended by the MH. The mean prevalence of MTCT was 5.9%. Despite the efforts exerted by the MH, the HIV algorithm noncompliance still occurs, and the vertical transmission rate is higher than 2%. These data reinforce the need to intensify the surveillance, to improve the information and the follow-up of pregnant women, and to rescue those responsible who do not strictly comply with the algorithm proposed by the MH.

**Keywords.** infectious disease transmission, vertical, HIV, diagnostic techniques and procedures.

### RESUMO

A epidemia do HIV no Brasil tem afetado de maneira especial as mulheres e trouxe, como um novo desafio a ser enfrentado, o controle da transmissão vertical (TV) do HIV. O objetivo deste estudo foi de avaliar o cumprimento ao algoritmo preconizado pelo Ministério da Saúde (MS) no diagnóstico de crianças nascidas de mães HIV positivas, acompanhadas no Centro de Laboratório Regional Instituto Adolfo Lutz de São José do Rio Preto-X, e avaliar a ocorrência de TV. Foram coletados dados do Sistema de Informação e Gestão Hospitalar (SIGH) e do Sistema de Controle de Exames Laboratoriais da Rede Nacional de Contagem de Linfócitos T CD4<sup>+</sup> e Carga Viral (SISCEL) no período de janeiro de 2009 a dezembro de 2014. Foram cadastradas 265 crianças, 141 (53,2%) eram do sexo masculino e 124 (46,8%) feminino. Destas, 217 (81,9%) completaram o algoritmo preconizado pelo MS. A média da prevalência de TV foi de 5,9%. Apesar dos esforços do MS, há descumprimento no algoritmo e a taxa de TV é maior que a meta de 2%. Os dados reforçam a necessidade de intensificar a vigilância, melhorar a informação e acompanhamento de gestantes e resgate dos responsáveis que não cumprem o algoritmo do MS.

**Palavras chave.** transmissão vertical de doença infecciosa, HIV, técnicas e procedimentos diagnósticos.

## INTRODUCTION

The acquired immunodeficiency syndrome (aids) epidemic has stabilized in Brazil over the last ten years with an average of 20.7 cases per 100,000 inhabitants. In the same period, the Human Immunodeficiency Virus (HIV) detection rate in the pregnant women increased by around 28.6%. Thus, concern over the mother-to-child transmission of HIV (MTCT) issue has been growing<sup>1</sup>.

MTCT may occur during the pregnancy (35%) or at delivery (65%), with an increased risk from 7% to 22% of transmission during breastfeeding. The preventive measures may reduce this latter transmission to the levels from 0% to 2.0%<sup>2</sup>.

From the beginning of the epidemic in 1980 to June 2016, 842,710 aids cases were notified in Brazil, and by December 2015, 303,353 deaths were occurred in patients of all of age groups<sup>1</sup>. As of June 2012, there were 17,539 cases in under 5-year-old children and 4,435 cases in children between 5 and 9 years old. Since October 1996, the National Program, nowadays the STD/Aids and Viral Hepatitis Department of the Ministry of Health, has recommended the prophylaxis against MTCT for all of HIV-positive pregnant women and for newborns exposed to HIV. This strategy has reduced the number of MTCT cases in Brazil, even though the rate remains above the goal of elimination. Data from a Brazilian multicenter collaborative study reported the MTCT rate of 7.5% in 2003 and 2004<sup>3</sup>.

A study performed by Succi et al<sup>4</sup> and the Epidemiological Bulletin of the Ministry of Health<sup>1</sup> reveal that despite the occurrence of a fall in the MTCT rate, differences were found out among the geographic regions of Brazil reflecting the cultural, economic and social diversity, as well as the access to health services.

Since 2002, a significant decrease was observed in the number of aids cases due to MTCT; but in the recent years, this rate has stabilized at an unsatisfactory level of around 500 cases/year in under 5-year-old children<sup>3</sup>.

In 2012, MTCT was the form of exposure to HIV in 99.6% of under 13-year old patients.

In under 5-year-old children, MTCT has been considered responsible for approximately 100% of aids cases. Thus, in Brazil the incidence rate of aids in under 5-year-old children (per 100,000 inhabitants) has been regarded as proxy indicator of the MTCT rate in the country. The incidence rate of aids in under 5-year old children has been stable in Brazil at an average level of 3.5 per 100,000 inhabitants; but a large variation among the federation districts and among the regions has been found<sup>3</sup>.

Data from the meta-analysis by Drake et al<sup>5</sup> corroborate this information, showing that the MTCT rate was high (22.7%) for the group of pregnant and puerperal women with incident infections. This group also presented a 2.8-fold higher risk of transmission when compared to women with chronic infections, confirming that the prophylaxis with antiretroviral drugs is effective for preventing MTCT.

According to the new clinical protocol published by the Brazilian Ministry of Health (BMH)<sup>3</sup>, the early identification of vertically infected children is crucial for starting the antiretroviral therapy, the prophylaxis against opportunistic infections and the management of infectious complications and nutritional disorders. The transplacental passage of maternal anti-HIV IgG antibodies, mainly in the third trimester of gestation, interferes in the diagnosis of vertical infection. Maternal antibodies may persist until the infant is 18 months of age. Therefore, the detection of HIV antibodies is not sufficient for diagnosing children younger than 18 months of age. Hence, it is necessary to perform virological tests, such as viral RNA quantification, a test provided by the BMH. The laboratory diagnosis of HIV MTCT follows the algorithm updated by the BMH<sup>3</sup>.

All of these data demonstrate that MTCT continues to occur in several regions of Brazil and of the world, in spite of the efforts to eradicate the transmission with the launch of the Global Plan to Eliminate New HIV Infections in Children by the year 2015, proposed by the Joint United Nations Program on HIV/aids<sup>6</sup>. The regional investigations and the follow-ups are necessary, for better understanding the reality of each region.

The objective of the present study was to assess the compliance with the algorithm, recommended by the BMH for diagnosing the children born to HIV-positive mothers followed-up in the Institute Adolfo Lutz - Regional Laboratory of São José do Rio Preto X-SP, and to evaluate the occurrence of mother-to-child transmission.

## MATERIAL AND METHODS

This cross-sectional descriptive study collected data on the CD4<sup>+</sup>T-cell count and the viral load by the System for Controlling Laboratory Examinations (SISCEL) and the System for Hospital Management (SIGH). The data from children aged from 1 to 18 months born to HIV-positive others, who performed the HIV viral load test at the Institute Adolfo Lutz - Regional Laboratory of São José do Rio Preto-X during the period from January 2009 to December 2014 were analyzed. This laboratory

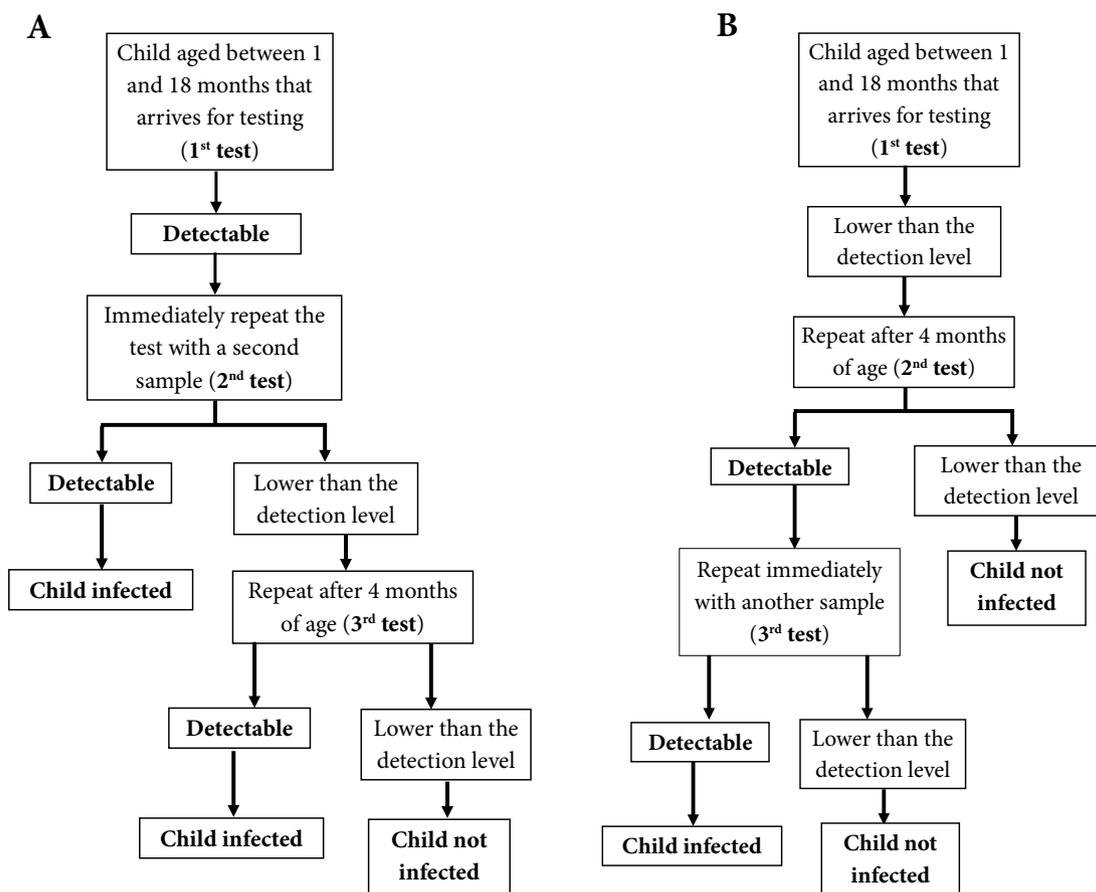
is the reference center for Regional Health Departments XV, which is comprised of 102 municipalities located in the northwest region of São Paulo State.

### Evaluation of adherence to the algorithm

All of the records of children aged 1 to 18 months were evaluated regarding the compliance with the algorithm formally approved by of the BMH<sup>3</sup> ( ).

### Evaluation of the occurrence of mother-to-child transmission

The viral load (VL) results detected in samples from children were analyzed for investigating the occurrence of MTCT. According to the new clinical protocol of the BMH, the detectable viral load below 5,000 copies/mL should be carefully analyzed, and the sample has to retested be repeated for possible false results.



**Figure 1.** Algorithm of tests used for the diagnosis of HIV in children aged between 1 and 18 months, born of HIV positive mothers. A) Viral load detectable in the 1<sup>st</sup> test. B) Viral load below the limit of detection in the 1<sup>st</sup> test

An under 18-month-old child with two undetectable viral load results, the second one being performed after four months of age, this case is considered non-HIV infected and no longer “probably uninfected”.

Therefore, the results found in this study were presented according to the following recommendations: children with undetectable viral load, being possibly false-positive children (viral load results <5,000 copies/mL) and children with detectable viral load (viral load > 5,000 copies/mL).

The HIV transmission was calculated by the proportion of the number of newborns with detectable viral load (viral load >5,000 copies/mL), divided by the total number of newborns per studied year. The average was calculated by the sum of the rates observed per year, divided by the number of evaluated years.

### Statistical analysis

The results found in this study are presented according to the absolute frequency and their occurrence over the years. The statistical program EPI Info version 7.1 was used for analyzing the data.

### Ethical considerations

This project was submitted (n° 841.188) and it was approved by the Ethics Committee of the Central Instituto Adolfo Lutz - São Paulo, SP, in accordance with the National Health Council - MH (NHC) Resolution 466 of December 12, 2012.

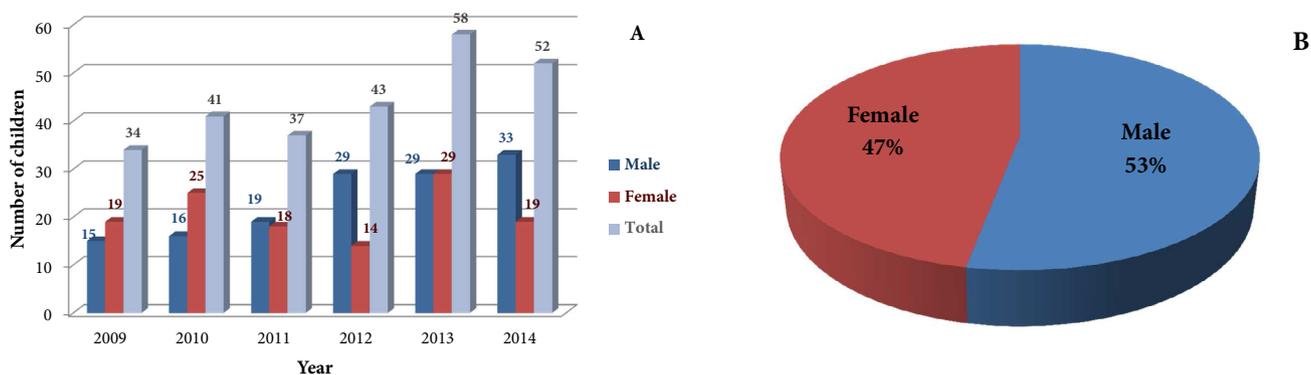
Considering that only the registered data were evaluated and that there was no possibility of harm to the patients, a waiver was granted in respect to the necessity of informed written consent.

## RESULTS

In the evaluated period, 265 children aged from 1 to 18 months were registered, being 141 male and 124 female (53% and 47%, respectively;  $p$ -value>0.05). The number of evaluated children grew progressively over the years. The distribution of children by sex is shown in

On average 49.8% (132/265) of the guardians took two months to start the evaluation (1<sup>st</sup> collection). The first sample collection was done in the 1<sup>st</sup>, 3<sup>rd</sup> and 4<sup>th</sup> months of age in 18% (49/265), 10% (28/265) and 7% (20/265) of children, respectively. The remaining children were tested from six (0.5%) to 11 months (2%). Only one child had its first collection after 18 months of age.

Regarding the collection of the second sample, only 2.3% (5/217) of the guardians followed the algorithm and returned within two months; 11% (25/217) returned in three months, 41% (89/217) returned after four months and about 18% (39/217) and 9% (19/217) in five and six months, respectively. The other guardians returned for the second test from 7 (3.7%) to 20 months (0.5%).



**Figure 2.** A) Number of children born to HIV-positive mothers who performed the viral load in CLR IAL São José do Rio Preto – X, from January 2009 to December 2014. B) Distribution of children according to sex

As for the adhesion to the BMH algorithm, the majority (82% - 217/265) completed all of the stages of the testing algorithm ( ).

Considering the children who presented positive results in the first sample, 33% did not return within the period of time recommended by the algorithm, that is, a second sample collection should be performed immediately upon receiving the result.

In the present study, no child with detectable viral load <5,000 copies (false positive) was observed in any of the analyzed samples (1<sup>st</sup> and 2<sup>nd</sup> collections). The detectable and undetectable viral load results are shown in .

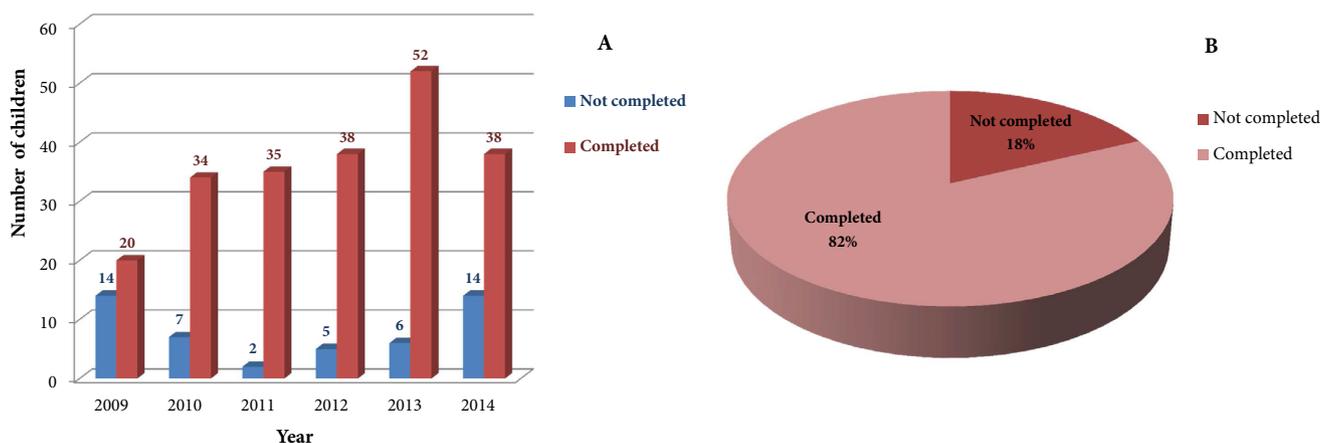
When assessing the MTCT, the prevalence rates observed at each year ranged from 2.3% to 10.8% with the overall mean of 5.9%. shows the annual prevalence distribution of MTCT.

## DISCUSSION

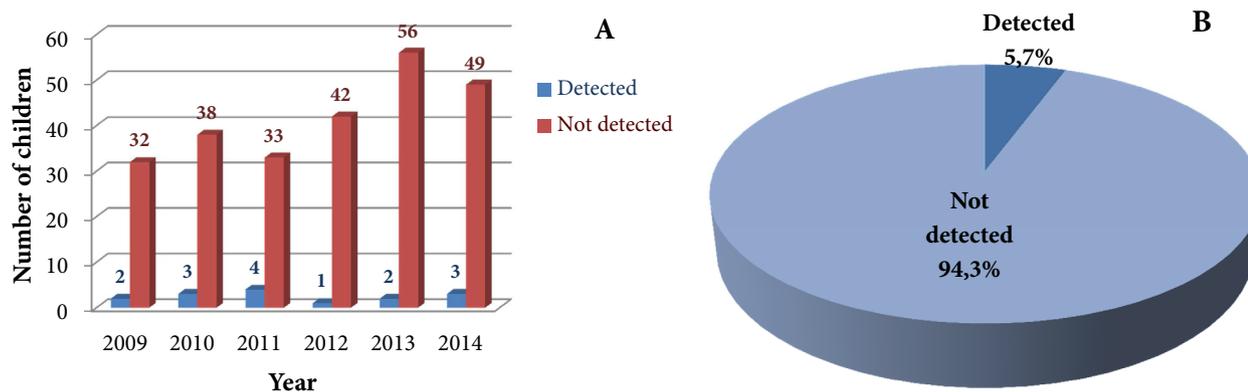
Brazil was the first country to develop and to implement the measures to prevent MTCT<sup>7,8</sup>.

The algorithm was instituted in 2002, according to the Guide for Clinical Treatment of HIV Infection in Children - BMH/Health Surveillance Secretariat<sup>9</sup>. Since then, attempts to reduce the rate of MTCT in the country has been made. In 2006, the BMH included in their Pact for Life a pledge to reduce the maternal and infant mortality, and being one of the priorities the reduction of the mother-to-child transmission rate of HIV and syphilis<sup>6</sup>.

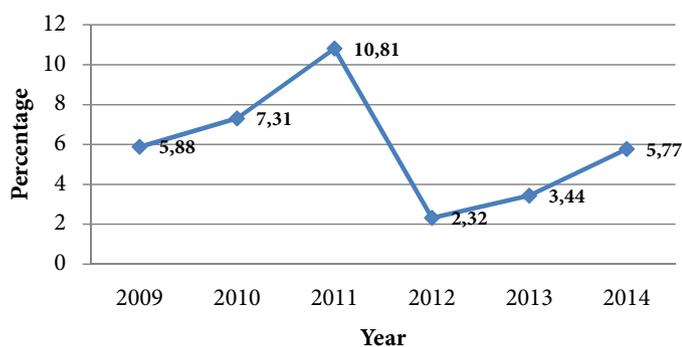
In the present study, 265 children were analyzed with no significant difference between genders. According to Vermelho et al<sup>10</sup>, no sex differences



**Figure 3.** Compliance with the algorithm designed by the Ministry of Health. A) Number of the children by year evaluated. B) Overview of the study



**Figure 4.** HIV viral load results in children from 1 to 18 months born of HIV-positive mothers, performed in CLR IAL São José do Rio Preto - X, from January 2009 to December 2014. A) Distribution by year. B) Overview of the study



**Figure 5.** Distribution of the annual prevalence of MCTC in children born from HIV-positive mothers who performed viral load in the CLR IAL São José do Rio Preto - X, from January 2009 to December 2014

were observed throughout the study period (1990-1999), although in the early years of the epidemic, the predominance of male patients occurred due to hemophilia.

A survey carried out from 2001 to 2006 in the western region of São Paulo State<sup>11</sup> showed that 20% of HIV-positive mothers had not performed the HIV tests in their children even at eight months after birth. The current study shows that this time has been reduced to two months.

Regarding the compliance with the algorithm of BMH, 18% of the analyzed children did not complete all of the testing steps. These data corroborate the studies performed by Gouveia et al<sup>12</sup>, Succi<sup>4</sup> and Matida et al<sup>13</sup>. However, the percentage was lower when compared to the studies by Patrício et al<sup>14</sup> and Vasconcelos et al<sup>15</sup>, who observed 28% and 31%, respectively, without following-up after delivery. According to Moura et al<sup>16</sup> some seropositive mothers still believe that their children will be born healthy, free of IV contamination and that the post-natal treatment is fully effective, thereby justifying the non-compliance with the algorithm.

Regarding MTCT, the rates observed in this study (mean 5.9%) corroborate those found in other studies<sup>11,17-20</sup>. Although the occurrence of the decrease in relation to both evaluations, previous to the BMH program<sup>21</sup> and the more recent studies<sup>14,22</sup>, the goal of the Brazilian government established at 2% of children infected through MTCT until 2015 has not yet been achieved<sup>6</sup>.

According to the BMH, the variation in the MTCT rates is mainly related to the regions of the country, followed by the mother age and schooling. In the last ten years, 42.7% reduction in the MTCT rate occurred in Brazil, but the states of Roraima and of Rio Grande do Sul have shown rates considered very high<sup>1</sup>.

According to Burger<sup>18</sup>, the rate in the city of Curitiba which was 5.1% in 1999 fell to 2.5% in 2009, because of the preventative measures that were instituted. In another study carried out in Sorocaba, São Paulo State which established the “Mother-to-child Transmission Zero” Program, more than ten years ago, the rate dropped to 0.17%, that is, almost to zero<sup>23</sup>.

The low adherence to the algorithm observed in this study and the high MTCT rate, might be due to the lack of information of the professional or of the children guardian. On the other hand, possibly the child registration changed due to the adoption or even the child death; thus, the second sample collections might not have been done or even identified.

The stable reduction of MTCT cases indicates that still much work has to be done, and that it is still not feasible to achieve the BMH goal in the short term. This situation occurs because many factors influence on the results, such as: the diagnosis and the delayed treatment of pregnant women; the lack of adherence to treatment; the special attention given to pregnant women who use illicit drugs, and they currently represent a major problem in the MTCT elimination<sup>24</sup>. The study performed by Lima et al<sup>25</sup> highlights the vulnerability of young pregnant women with low socioeconomic and social resources, who start late the prenatal care and have high viral loads. These conditions have been the great challenge to the country public health services for eliminating MTCT.

This information reinforces the importance of developing the focused surveillance, the active searches and the rescue of patients who do not adhere to all of the steps of the algorithm recommended by the BMH, in order to eliminate the MTCT in the region analyzed in the present study and throughout the country.

## CONCLUSION

Despite all the efforts of the BMH, a lack of adherence still occurs by those responsible for complying with the HIV-1 testing algorithm for the diagnosis of children born to mothers carrying the virus. In the present study, 18% of non-compliance with the algorithm were detected.

Although 82% of the cases complied with the algorithm (two sequential samples), the majority (97.7%) did not meet the recommended deadlines, and among the children who showed positive results detected in the first sample, 33% did not return immediately to collect the second sample.

The services where the patients have been attended and the work performed with pregnant women still have not achieved the goal of the BMH, concerning the MTCT rate 2%, as in the present study the observed mean was 5.9%.

Although this study did not investigate those responsible for this situation, it is considered essential to develop the special measures for mothers who use illicit drugs, because they represent the major problem for potentially maintaining the rate of MTCT.

These data reinforce the need to intensify the surveillance, to improve information and the follow-up of HIV-positive pregnant women, in order to promote an active search and to rescue the children whose guardians do not complete all of the steps of the diagnostic algorithm proposed by the BMH.

## ACKNOWLEDGEMENT

Dra. Susilene Maria Tonelli Nardi for her collaboration in the statistical analysis.

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