0021-7557/10/86-06/
Jornal de Pediatria
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Persistent operational challenges lead to non-reduction in maternal-infant transmission of HIV

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Abstract

Objective: To determine the impediments to the effective reduction of maternal-infant transmission of HIV in the municipality of Campos dos Goytacazes, RJ, Brazil.

Methods: This is a cohort study, with medical follow-up, of pregnant women with confirmed diagnosis of HIV infection, and their infant children, assisted at the Municipal Specialized Service of Sexually Transmitted Diseases/AIDS from January 2004 to April 2007. Information regarding exposure and outcome variables was collected from their medical records. Frequencies of variables were determined and bivariate analysis performed for exposure factors and transmission of HIV. Relative risks of HIV transmission associated with exposure variables were calculated using 95% confidence intervals. Statistical significance of risk associations was evaluated.

Results: Seventy-eight mother-child pairs were studied; the rate of maternal-infant transmission of HIV was 7.7%. Variables showing significant association with maternal-infant transmission of HIV were the non-utilization of antiretrovirals for prophylaxis or treatment during pregnancy (RR = 21.00; 95%CI 2.64 to 166.74, p = 0.001) and diagnosis of maternal disease after pregnancy (RR = 6.80; 95%CI 1.59 to 29.17, p = 0.025). New pregnancies in women with other children also exposed to HIV occurred in 19.12 % (15/78) of cases.

Conclusions: There was no reduction in the rate of maternal-infant transmission of HIV in the period 2004-2007 in relation to the preceding triennium. The following were recognized as impediments to the effective reduction of maternal-infant transmission of HIV: low prenatal screening coverage of maternal HIV infection, impairing maternal treatment or prophylaxis; and the incorrect use of the rapid screening test at admission for delivery.

J Pediatr (Rio J). 2010;86(6): Antiretrovirals, HIV, newborn, maternal-infant transmission.

Introduction

In Brazil, the rate of HIV infection among pregnant women is 0.6%,[1] and preventing maternal-infant transmission (MIT) of HIV is a directive from Coordenação Nacional de DST e AIDS (National STD and AIDS Program).[2]

In the absence of any sort of intervention, rates of MIT of HIV are around 30 percent, though they may be cut down by 66 percent with the use of Zidovudine from the 14th week of pregnancy onwards, intravenously during delivery, and administered orally to the newborn during the first six weeks of life (Protocol ACTG 076).[3] Its use for shorter periods also decreases rates of MIT of HIV.[4]

In developed countries, where every strategy is employed to prevent MIT of HIV, transmission rates range from 1 to 2 percent. In the developing world, high perinatal

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No conflicts of interest declared concerning the publication of this article.

Suggested citation: Fernandes RC, Ribas GF, Silva DP, Gomes AM, Medina-Acosta E. Persistent operational challenges lead to non-reduction in maternal-infant transmission of HIV. J Pediatr (Rio J). 2010;86(6):

Financial support: Secretaria Municipal de Saúde de Campos, Programa Nacional de DST/Aids de Campos dos Goytacazes, Brazilian Ministry of Health. UNESCO.

Manuscript submitted 07.12.10, accepted for publication 09.09.10.

doi:10.2223/JPED.2040

transmission persists due to the difficulty in diagnosing all infected pregnant women and submitting them to treatment or prophylaxis with antiretrovirals; and due to postpartum transmission via breastfeeding, which remains a major challenge.[5]

In Brazil, Protocol ACTG 076 has been in use since 1996. Universidade Federal do Rio de Janeiro had an especially successful experience with the protocol, and its Programa de Assistência Integral à Gestante HIV (Full Health Care for Pregnant Women with HIV Program) reported a rate of MIT of HIV of 1.6 percent.[6] With triple therapy for pregnant women, the study by Escola Paulista de Medicina recorded absence of HIV infection in 111 children exposed to the virus.[7] More recently, a multicenter study by Sociedade Brasileira de Pediatria reported a decrease in MIT of HIV from 16 percent in 1995 to 2.4 percent in 2002 in the state of São Paulo.[8]

Starting in 1999, the STD/AIDS Program of the city of Campos dos Goytacazes, Rio de Janeiro, implemented the Municipal Program for Prevention of MIT of HIV, following Brazilian Ministry of Health guidelines for pregnant women and children exposed to the virus.[9]

From January 2001 to December 2003, the HIV infection rate among pregnant women in the municipality was 0.5 percent, close to the national average of 0.6 percent.[10,11] From October 1999 to June 2004, 44 mother-child pairs submitted to Protocol ACTG 076 were tracked.[12] Coverage of anti-HIV testing ranged from 28 percent in 2001 to 46 percent in 2003, with MIT of HIV rates of 6.8 percent during the period.[12]

The present study sought to describe the changes that took place from 2004 to 2007, in an attempt to review the strategies used to warrant a more effective prevention of MIT of HIV in the future.

Methods

Study design

This was an observational, prospective, longitudinal, analytic, concurrent cohort study that sought to determine the impediments to the effective reduction of MIT of HIV in the municipality of Campos dos Goytacazes, Rio de Janeiro, Brazil

Research subjects

The research included all pregnant women with confirmed diagnosis of HIV infection, as well as their infant children, as long as they completed HIV infection exams, assisted at the Municipal Specialized Service of Sexually Transmitted Diseases/AIDS in Campos dos Goytacazes, Rio de Janeiro, Brazil, from January 2004 to April 2007.

Data collection

Data were collected through a review of mothers' and infants' medical records. Information regarding the relevant variables was recorded in a questionnaire developed especially for this survey. Occurrence of MIT of HIV was considered the dependent variable. The following were considered exposure variables: delivery route, rupture of membranes, birth weight, breastfeeding, maternal age, previous knowledge of risk of HIV infection, maternal education, time of diagnosis of HIV infection relative to pregnancy, viral load, CD4 counts, and maternal prophylaxis or treatment. The data from the questionnaire were managed using the application EpiData version 3.1[13] and analyzed using application EpiData Analysis V2.2.1.171.

Statistical analysis

Frequencies of variables were determined and bivariate analysis performed for exposure and dependent variables. As measure of outcome, relative risks of MIT of HIV associated with exposure variables were calculated using 95% confidence intervals (95%CI), excluding cases in which information about variables were not available and those for which there were no maternal viral load and CD4 exams. Due to the small sample size, Fisher's exact test was used to assess statistical significance of potential risk associations. The estimate of total pregnant women in the municipality comes from the "number of live births" indicator for the city for 2004-2006.[14]

Ethical considerations

The present study was approved by the Research Ethics Committee of Faculdade de Medicina de Campos.

Results

During the study period, on average 3,692 pregnant women received medical assistance annually, which corresponds to half the total number of pregnant women in the municipality, with little progress in recruitment throughout the study period (Table 1).

The cohort had greater use of cesarean sections, and predominant rupture of membranes at delivery and birth weight equal to or above 2,500 g, all variables associated with lower rates of MIT of HIV (Table 2).

Low maternal age (< 30 years old) was predominant, as was low education (< or equal to complete secondary education). Most pregnant women were aware of the risk of MIT of HIV and its prevention. Diagnosis of maternal disease before pregnancy was 38.5 percent and confirmed during the prenatal period in 48.7 percent of cases. When diagnosis of maternal infection was performed during the postpartum period, MIT of HIV was statistically significant.

Table 1 - Number of pregnant women assisted at the Centro de Testagem e Aconselhamento of the city of Campos dos Goytacazes, Rio de Janeiro, STD/AIDS Program and estimate of total number of pregnant women in municipality from the "number of live births" indicator for the city[14]

Total number of pregnant women	Year			Annual mean
	2004	2005	2006	
In city	7,659	7,558	7,398	7,538
Treated at CTA	3,337	3,879	3,861	3,692
Assistance coverage (%)	43.6	51.3	52.2	49.0

CTA = Centro de Testagem e Aconselhamento.

Not breastfeeding consists in a protective factor for MIT of HIV (Table 3).

Maternal viral load and CD4 counts, when assessed, had no statistically significant association with MIT of HIV. Non-use of prophylaxis or treatment during pregnancy had a statistically significant association with MIT of HIV (Table 4).

At endpoint, the investigation on MIT of HIV found that six children exposed to the virus were infected, the transmission rate being 7.7 percent. We analyzed their medical records to explain why each of the six infants was infected. Three mothers were diagnosed by rapid anti-HIV screening test: one before delivery, and the other two postpartum. In the first case, the child was born preterm, weighing 1,930 g, and cesarean section was performed after rupture of membranes. In the other two cases, mothers did not receive Zidovudine intravenously during delivery; one delivered vaginally, the other by cesarean section after rupture of membranes, and both infants were breastfed. In the fourth case, maternal HIV infection was diagnosed during pregnancy; the patient received triple therapy with Zidovudine, Lamivudine and Nelfinavir, delivered by cesarean section, and did not breastfeed. In this case, poor adherence to treatment on the part of the mother was implicated as cause. In the fifth, the patient had confirmed diagnosis before pregnancy and had been part of multiple treatment plans, always with poor compliance. Elective cesarean section was performed on the 38th week; the mother, with high viral load and severe immunodepression, suffered reactivation of toxoplasmosis and died.[15] The newborn, as well as infected with HIV, was also diagnosed with congenital toxoplasmosis. The case is a good example of what should be our greatest challenge in coming years: providing care to pregnant women in advanced stages of the disease, as well as treatment and follow-up for their infected children.[16] The sixth infected child was delivered vaginally, and her mother was also diagnosed in the postpartum period using rapid screening test. At 9 months old, her first viral load was undetectable, and follow-up was interrupted. At 3 years old, when diagnosis of HIV infection for her sister was confirmed, the girl was tested once again and serology results came back positive; the attending clinician learned her mother had resumed breastfeeding.

Table 2 - Relative risks of maternal-infant transmission of HIV associated with delivery and newborn exposure variables

Variable	Total , n (%)	MIT of HIV		p
		n (%)	RR (95%CI)	
Delivery route				
Cesarean section	62 (79.5)	4 (6.5)	0.52 (0.10-2.57)	0.596
Vaginal	16 (20.5)	2 (12.5)	1.94 (0.39-9.65)	0.596
Rupture of membranes*				
At birth	52 (69.3)	3 (5.8)	0.66 (0.12-3.71)	0.639
≤ 4 hours	10 (13.3)	1 (10)	1.63 (0.20-13.11)	0.521
> 4 hours	13 (17.3)	1 (7.7)	1.19 (0.14-9.82)	1.000
Uninformed	3 (3.8)	1 (33.3)	5.00 (0.82-30.57)	0.216
Birth weight (g)*				
< 2,500	13 (17.3)	1 (7.7)	1.59 (0.18-14.10)	0.541
≥ 2,500	62 (82.7)	3 (4.8)	0.63 (0.07-5.58)	0.541
Uninformed	3 (3.8)	2 (66.7)	12.50 (3.60-43.40)	0.015

MIT = maternal-infant transmission; RR = relative risk.
* Cases with uninformed birth weight and rupture of membranes were excluded from the calculation of MIT rates.

Table 3 - Relative risks of maternal-infant transmission of HIV associated with maternal exposure, socioeconomic and diagnosis variables

Variable	Total , n (%)	MIT of HIV		p
		n (%)	RR (95%CI)	
Maternal age (years)				
< 30	59 (75.6)	5 (8.5)	1.61 (0.20-12.94)	1.000
≥ 30	19 (24.4)	1 (5.3)	0.62 (0.08-4.99)	1.000
Maternal education*				
≤ complete secondary education	65 (86.7)	6 (9.2)		1.000
> complete secondary education	10 (13.3)	0 (0.0)		1.000
Uninformed	3 (3.8)	0 (0.0)		1.000
Knowledge of risk of MIT of HIV				
Yes	51 (65.4)	2 (3.9)	0.26 (0.05-1.35)	0.174
No	27 (34.6)	4 (14.8)	3.78 (0.74-19.32)	0.174
Time of maternal diagnosis				
Before pregnancy	30 (38.5)	1 (3.3)	0.32 (0.04-2.61)	0.397
During pregnancy	38 (48.7)	2 (5.3)	0.53 (0.10-2.71)	0.676
After pregnancy	10 (12.8)	3 (30.0)	6.80 (1.59-29.17)	0.025
Breastfeeding				
Yes	8 (10.3)	3 (37.5)	8.75 (2.11-36.32)	0.013
No	70 (89.7)	3 (4.3)	0.11 (0.03-0.47)	0.013

MIT = maternal-infant transmission; RR = relative risk.
* Cases with uninformed maternal education were excluded from the calculation of MIT rates.

Table 4 - Relative risks of maternal-infant transmission of HIV associated with exposure variables for maternal HIV infection and antiretrovirals used

Variable	Total , n (%)	MIT of HIV		p
		n (%)	RR (95%CI)	
Maternal viral load*				
Not performed	62 (79.5)	4 (6.5)	0.52 (0.10-2.57)	0.597
Undetectable	5 (31.3)	0 (0.0)		1.000
≤ 1,000 copies/mL	2 (12.5)	0 (0.0)		1.000
> 1,000 copies/mL	9 (56.3)	2 (22.2)		0.475
Maternal CD4*				
Not performed	58 (74.4)	4 (6.9)	0.69 (0.14-3.48)	0.643
> 500 cel/mL	8 (40.0)	1 (12.5)	1.50 (0.11-20.68)	1.000
200-499 cel/mL	8 (40.0)	0 (0.0)		0.495
< 200 cel/mL	4 (20.0)	1 (25.0)	4.00 (0.31-51.03)	0.368
Antiretroviral therapy during pregnancy				
No therapy	15 (19.2)	5 (33.3)	21.00 (2.64-166.74)	0.001
Zidovudine	31 (39.7)	0 (0.0)		0.076
Triple therapy	32 (41.0)	1 (3.1)	0.29 (0.04-2.35)	0.392

MIT = maternal-infant transmission; RR = relative risk.
* Cases with uninformed maternal viral load and CD4 were excluded from the calculation of MIT rates.

Discussion

In 2007, an eight year project focused on preventing MIT of HIV in the municipality of Campos dos Goytacazes was completed. The project overcame several well known obstacles: 1) awareness of need to request anti-HIV serology during pregnancy; 2) extending testing initially concentrated in a single health care unit; 3) integration with Programa de Saúde da Mulher e de Saúde da Família (Woman and

Family Health Program), as discussed in the literature;[12,17] 4) municipal responsibility for CD4 and viral load dosages, at the moment available for all pregnant women seeking assistance; and 5) use of rapid anti-HIV screening tests in previously unexamined pregnant women.

Despite the effort, there was no decrease in the rate of MIT of HIV in the 2004-2007 triennium (7.7%) in relation to the 2001-2003 triennium (6.8%).[12]

From January 2004 to April 2007, 81 mother-child pairs were studied, three of whom were excluded from the final analysis, two because the infants died in the first months of life and one because of loss of patient follow-up. Cesarean sections were predominant, confirming their protective power over MIT of HIV;[18] the same was found for rupture of membranes during delivery.

In cases with birth weight below 2,500 g, relative risk of MIT of HIV was high. This points to possibility of more advanced maternal disease, as well as treatment with protease inhibitors, which are associated with preterm birth and, consequently, low birth weight.[19-21]

The pregnant women in this study were predominantly young, 30 years old or less, and had low education levels, matching current epidemiological trends in Brazil, i.e., the feminization and pauperization of the disease.[2,12,22] Some were younger than 20, which imposes an additional challenge to the research. At that age range, there are more Brazilian women infected with HIV than men, a particularly grave problem in the context of increased teenage pregnancy and low adherence to prenatal care and treatment in this age group.[12]

Not all pregnant women were aware of the potential for MIT of HIV, a fact that highlights the need to stress that possibility at every opportunity (waiting room in outpatient facilities, hospital environments, doctors' offices, etc.).

Regarding time of maternal diagnosis, the present study can show very little increase in recruitment of pregnant women before delivery and greater usage of rapid screening tests at delivery in relation to the period before 2004.[12] The situation calls for greater awareness of the importance of its use soon after pregnant women are admitted to the hospital, thus enabling the immediate application of prophylaxis measures. The nonperformance of immediate rapid screening tests led to high rates of MIT of HIV, and the association was statistically significant.

The World Health Organization strongly contraindicates breastfeeding in cases of maternal HIV infection and in locations where milk-based formula is available.[23] In the present cohort, diagnosis of infection using the rapid screening test postpartum enabled infants to be breastfed, impacting MIT of HIV.

The importance of diagnosing HIV infection before pregnancy was confirmed, since it enables the use of Zidovudine or triple antiretroviral therapy. Without the use of any prophylaxis or therapy during pregnancy, rates of MIT of HIV reach 33.3 percent, compared to 0 percent for the group receiving Zidovudine and 3.1 percent for the group receiving triple therapy. The higher transmission value of the last group is probably correlated with its late start, incomplete adherence to the treatment regimen, more severe and prolonged maternal disease, and the pharmacokinetics of antiretrovirals during the last trimester of pregnancy.[24]

The rate of MIT of HIV of 7.7% determined in this study is very high when compared to that of other studies: in Spain (1.42%),[25] a rural province in China (1%),[26] the European Collaborative Study (1.72%),[24] and South Africa (4.9%).[27] It is also high when compared to other Brazilian studies,[6-8] and its determining factors were clearly defined by the analysis of individual cases of infected children: late diagnosis of maternal infection, incorrect use of rapid screening test, failure to contraindicate breastfeeding, low adherence to antiretroviral therapy by pregnant women, and persistence of breastfeeding after diagnosis of maternal disease.

Another important aspect is the occurrence of new pregnancies in the context of previously known maternal HIV infection. Our cohort included 15 such cases. The fact underscores the importance of recommending the use of preservatives and/or other birth control resources, as well as follow-up by multidisciplinary teams.

In conclusion, the challenge of preventing MIT of HIV remains, despite all the hard work of health care professionals. The following factors determined the non-reduction of MIT of HIV: low coverage of prenatal anti-HIV testing and incorrect use of rapid screening tests upon admission of untested pregnant women for delivery. These obstacles will only be overcome by the concerted efforts of health care professionals, managers, and the government. Each new child infected with HIV by MIT should be faced as a sentinel failure event in care provided to pregnant women, and requiring judicious analysis of the situation.

Acknowledgments

To the pregnant women and their children who took part in this study. To the members of the Campos dos Goytacazes Municipal STD/AIDS Program and Specialized Service of Sexually Transmitted Diseases/AIDS.

References

1. Ministério da Saúde, Brasil. Secretaria de Vigilância em Saúde. Programa nacional de DST e Aids. Boletim Epidemiológico - Aids e DST. Brasília: Ministério da Saúde; 2007. [Online] http://www2.aids.gov.br/data/documents/storedDocuments/%7BB8EF5DAF-23AE-4891-AD36-1903553A3174%7D/%7B721527B6-FE7A-40DF-91C4-098BE8C704E0%7D/Boletim2007_internet090108.pdf. Acesso: 04/07/2010.

2. Ministério da Saúde, Brasil. Secretaria de Vigilância em Saúde. Programa nacional de DST e Aids. Boletim Epidemiológico - Aids e DST. Brasília: Ministério da Saúde; 2002. [Online] http://www2.aids.gov.br/data/documents/storedDocuments/%7BB8EF5DAF-23AE-4891-AD36-1903553A3174%7D/%7B3C849B6E-AF5E-48DE-9DC1-2AC2DBED6873%7D/bol_marco_2002.pdf. Acesso: 04/07/2010.
3. Sperling RS, Shapiro DE, Coombs RW, Todd JA, Herman SA, McSherry GD, et al. Maternal viral load, zidovudine treatment, and the risk of transmission of human immunodeficiency virus type 1 from mother to infant. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. N Engl J Med. 1996;335:1621-9.
4. Wade NA, Birkhead GS, Warren BL, Charbonneau TT, French PT, Wang L, et al. Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. N Engl J Med. 1998;339:1409-14.
5. Mofenson LM. Prevention in neglected subpopulations: prevention of mother-to-child transmission of HIV infection. Clin Infect Dis. 2010;50 Suppl 3:S130-48.
6. Nogueira SA, Abreu T, Oliveira R, Araujo L, Costa T, Andrade M, et al. Successful prevention of HIV transmission from mother to infant in Brazil using a multidisciplinary team approach. Braz J Infect Dis. 2001;5:78-86.
7. Succi RC. Avaliação da implementação da prevenção da transmissão vertical do HIV no Brasil: resultados e problemas enfrentados, a experiência da Escola Paulista de Medicina EPM/UNIFESP. In: Conferência Internacional sobre infecção pelo HIV em Mulheres e Crianças. Rio de Janeiro. Informed Eventos; 2002. p. 6-7.
8. Matida LH, da Silva MH, Tayra A, Succi RC, Gianna MC, Goncalves A, et al. Prevention of mother-to-child transmission of HIV in Sao Paulo State, Brazil: an update. AIDS. 2005;19 Suppl 4:S37-41.
9. Ministério da Saúde, Brasil. Secretaria de Vigilância em Saúde. Programa nacional de DST e Aids. Recomendações para profilaxia da transmissão vertical do HIV e terapia anti-retroviral em gestantes. Brasília: Ministério da Saúde; 2003. [Online] http://www.saude.rio.rj.gov.br/media/dstaids_consenso_gestante_2007.pdf. Access: 04/072010.
10. Araújo LC, Fernandes RC, Coelho MC, Medina-Acosta E. Prevalência da infecção pelo HIV na demanda atendida no Centro de Testagem e Aconselhamento na Cidade de Campos dos Goytacazes, Estado do Rio de Janeiro, Brasil, 2001-2002. Epidemiol Serv Saude. 2005;14:85-90.
11. Araújo LC. Prevalência da infecção pelo HIV no Centro de Testagem e Aconselhamento de Campos e transmissão materno-infantil do HIV no município de Campos dos Goytacazes, Rio de Janeiro [tese]. Campos dos Goytacazes (RJ): Universidade Estadual do Norte Fluminense Darcy Ribeiro; 2006.
12. Fernandes RC, Araújo LC, Medina-Acosta E. O desafio da prevenção da transmissão vertical do HIV no Município de Campos dos Goytacazes, Rio de Janeiro, Brasil. Cad Saude Publica. 2005;21:1153-9.
13. Lauritsen JM, Bruus M. EpiData Entry (version 3.1): A comprehensive tool for validated entry and documentation of data. Odense, Denmark: The EpiData Association; 2005.
14. Ministério da Saúde, Brasil. Secretaria de Vigilância em Saúde. Departamento de Análise de Situação de Saúde. Sistema de Informações sobre Nascidos Vivos - SINASC, Brasil, período 1994-2005. [Online] http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sinasc/cnv/nvbr.def. Access: 04/07/2010.
15. Fernandes RC, Vasconcellos VP, Araujo LC, Medina-Acosta E. Vertical transmission of HIV and Toxoplasma by reactivation in a chronically infected woman. Braz J Infect Dis. 2009;13:70-1.
16. Volmink J, Siegfried NL, van der Merwe L, Brocklehurst P. Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection. Cochrane Database Syst Rev. 2007;CD003510.
17. Souza Junior PR, Szwarcwald CL, Barbosa Junior A, Carvalho MF, Castilho EA. Infecção pelo HIV durante a gestação: Estudo-Sentinela Parturiente, Brasil, 2002. Rev Saude Publica. 2004;38:764-72.
18. Caesarean section and risk of vertical transmission of HIV-1 infection. The European Collaborative Study. Lancet. 1994;343:1464-7.
19. European Collaborative Study; Swiss Mother and Child HIV Cohort Study. Combination antiretroviral therapy and duration of pregnancy. AIDS. 2000;14:2913-20.
20. Grosch-Woerner I, Puch K, Maier RF, Niehues T, Notheis G, Patel D, et al. Increased rate of prematurity associated with antenatal antiretroviral therapy in a German/Austrian cohort of HIV-1-infected women. HIV Med. 2008;9:6-13.
21. Townsend CL, Tookey PA, Newell ML, Cortina-Borja M. Antiretroviral therapy in pregnancy: balancing the risk of preterm delivery with prevention of mother-to-child HIV transmission. Antivir Ther. 2010;15:775-83.
22. Kourtis AP, Lee FK, Abrams EJ, Jamieson DJ, Bulterys M. Mother-to-child transmission of HIV-1: timing and implications for prevention. Lancet Infect Dis. 2006;6:726-32.
23. World Health Organization. Rapid advice: revised WHO principles and recommendations on infant feeding in the context of HIV. Geneva: WHO Press; 2009. [Online] http://www.who.int/hiv/pub/paediatric/advice/en/index.html. Access: 02/092010.
24. European Collaborative Study. Factors associated with HIV RNA levels in pregnant women on non-suppressive highly active antiretroviral therapy at conception. Antivir Ther. 2010;15:41-9.
25. Fernandez-Ibieta M, Ramos Amador JT, Guillen Martin S, Gonzalez-Tome MI, Navarro Gomez M, Iglesias Gonzalez-Nicolas E. et al. Why are HIV-infected infants still being born in Spain?. An Pediatr (Barc). 2007;67:109-15.
26. Zhou Z, Meyers K, Li X, Chen Q, Qian H, Lao Y, et al. Prevention of mother-to-child transmission of HIV-1 using highly active antiretroviral therapy in rural Yunnan, China. J Acquir Immune Defic Syndr. 2010;53 Suppl 1:S15-22.
27. Hoffman RM, Black V, Technau K, van der Merwe KJ, Currier J, Coovadia A, et al. Effects of highly active antiretroviral therapy duration and regimen on risk for mother-to-child transmission of HIV in Johannesburg, South Africa. J Acquir Immune Defic Syndr. 2010;54:35-41.

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