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Review of the History and Current Status of Cell-Transplant Approaches for the Management of Neuropathic Pain

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Research Article

Progress towards Elimination of HIV Mother-to-Child Transmission in the Dominican Republic from 1999 to 2011

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In 1999, prevention of mother-to-child transmission (pMTCT) using antiretrovirals was introduced in the Dominican Republic (DR). Highly active antiretroviral therapy (HAART) was introduced for immunosuppressed persons in 2004 and for pMTCT in 2008. To assess progress towards MTCT elimination, data from requisitions for HIV nucleic acid amplification tests for diagnosis of HIV infection in perinatally exposed infants born in the DR from 1999 to 2011 were analyzed. The MTCT rate was 142/1,274 (11.1%) in 1999–2008 and 12/302 (4.0%) in 2009–2011 ($P < .001$), with a rate of 154/1,576 (9.8%) for both periods combined. This decline was associated with significant increases in the proportions of women who received prenatal HAART (from 12.3% to 67.9%) and infants who received exclusive formula feeding (from 76.3% to 86.1%) and declines in proportions of women who received no prenatal antiretrovirals (from 31.9% to 12.2%) or received only single-dose nevirapine (from 39.5% to 19.5%). In 2007, over 95% of DR pregnant women received prenatal care, HIV testing, and professionally attended delivery. However, only 58% of women in underserved sugarcane plantation communities (2007) and 76% in HIV sentinel surveillance hospitals (2003–2005) received their HIV test results. HIV-MTCT elimination is feasible but persistent lack of access to critical pMTCT measures must be addressed.

1. Introduction

HIV mother-to-child transmission (MTCT) continues to threaten child survival worldwide. Over two million children are infected with HIV, the vast majority infected by MTCT in low- and middle-income (LMI) countries [1, 2]. The persistence of HIV MTCT underscores the importance of increasing access to effective prevention of MTCT (pMTCT) strategies. Virtual elimination of HIV MTCT has been achieved in most industrialized countries, with declines of over 80%–90% in the number of cases of perinatally acquired HIV infection, and MTCT rates of under 2%–3% [3–5]. The use of highly active antiretroviral therapy ([HAART], defined as a regimen of three or more antiretrovirals from two or more classes), which is essential for elimination of MTCT and contributes to maternal health, has been shown to be cost effective compared to single-dose nevirapine in several LMI countries, including the Dominican Republic (DR) [6–8], but few data exist on the scalability of these measures or the current obstacles to eliminating MTCT in these countries [9–13].

The DR is home to 25% of persons living with HIV in the Caribbean, the second highest HIV-prevalence region in the world [1, 9, 10]. To assess progress towards MTCT elimination in this MI country, we analyzed data recorded at the time of collection of samples for virologic testing performed to determine whether perinatally exposed infants and young children had acquired HIV infection.

2. Methods

2.1. Population. Guardians of infants and children known or suspected of being perinatally HIV-exposed were asked if they would consent to diagnostic virologic testing of their children as part of pediatric care. The population tested included infants and children whose mothers were diagnosed with HIV infection before or during pregnancy, at delivery, and up to 25 months after the child's birth. Since HIV infection is a frequent cause of death among Caribbean women of reproductive age [10], HIV antibody testing was performed in orphaned and abandoned minors if maternal serostatus was unavailable. If the patient was seropositive, his/her guardian was offered virologic testing. A case of HIV infection acquired by MTCT was defined as an infant with a positive HIV nucleic acid amplification test [11]. Infants who had negative HIV nucleic acid amplification tests and had no symptoms of HIV infection were considered uninfected, but were followed until their HIV antibody tests were negative.

2.2. Prenatal and Infant pMTCT Practices. From 1999–2004, in La Romana province, in the region that formerly had the highest HIV prevalence in 2002 [12], nongovernmental organizations provided prenatal, perinatal and neonatal multidose zidovudine-containing regimens, with elective cesarean delivery and exclusive formula feeding, to HIV-infected mothers and their infants [6, 13]. During this time period, all data for this paper were collected from La Romana (Figure 1). Outside of La Romana, most HIV-infected women who were diagnosed during pregnancy

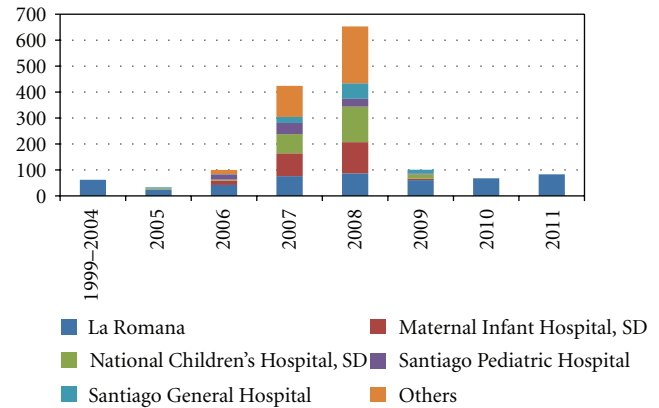


FIGURE 1: Perinatally HIV-Exposed Infants, by 34 Reporting centers, Dominican Republic, 1999–2011 “La Romana”: nongovernmental organization (NGO) located in La Romana, in southeastern Dominican Republic, provides prenatal care to 81–101 pregnant women living with HIV annually, approximately 30% of Haitian origin, and 20% from *bateyes* (underserved sugarcane plantation communities); virtually all (>97%) are low-income informally employed or unemployed [6, 13]. The NGO provides comprehensive care to approximately 1,300 persons living with HIV, of whom 130 are children. La Romana is a major sugar-producing area, with 100s of *bateyes* for workers. It is also a major tourist attraction. “Maternal Infant Hospital, SD”: public maternity hospital, located in Santo Domingo (SD) East, in the southern coast of the Dominican Republic [14], reports over 10,800 live births, at least 800 to women living with HIV. Most of the clients are low income, and over 20% may be of Haitian origin. The hospital provides comprehensive care to 90–101 children living with HIV. “National Children’s Hospital, SD”: Public children’s hospital located in SD, DR capital city, in the southern coast of the DR, reports >6,000 admissions per year, and evaluates 150–200 perinatally exposed infants per year. Most of the clients are low-income, and at least 20% are referred to tertiary services in the Children’s Hospital from other areas. The hospital provides comprehensive care to over 400 children living with HIV. “General Hospital, Santiago”: public general hospital located in the Northern city of Santiago de los Caballeros, reports approximately 23,000 admissions per year, of which 10,000 are obstetric, 90–120 of which are among women living with HIV. Although it is located in one of the more economically prosperous areas of the DR, it serves a diverse population and many clients are from impoverished border areas. The hospital provides comprehensive care to over 1,300 adults living with HIV, and prenatal care services to over 100 women living with HIV annually. “Pediatric Hospital, Santiago”: public children’s hospital located in the Northern city of Santiago de los Caballeros, reports over 3,000 admissions per year, and evaluates 50–60 perinatally exposed children per year. The hospital provides comprehensive care to approximately 140 children living with HIV. The other 29 centers that are represented in this population include two community based, three faith-based, and two other NGOs, and 22 public hospitals in the eastern, border, central, and southwestern provinces, including Elias Pina, El Seibo, and other low-healthcare-access areas [12, 15, 16].

were offered single-dose nevirapine at delivery, and exclusive formula feeding for their infants, according to national guidelines [17]. From 2004–2008, some women diagnosed with HIV infection before or during pregnancy started or continued HAART if they needed it for immunodeficiency;

others received single-dose nevirapine or a zidovudine-containing multidose regimen [13]. In 2008, the DR ministry of health issued guidelines recommending maternal HAART for pMTCT, whether or not the mother had evidence of immunodeficiency (Protocol for use of combined antiretroviral therapy in pregnant women living with HIV/AIDS, Ministry of Health, Santo Domingo, DR, October 2008). These guidelines called for initiating zidovudine and lamivudine combined with nevirapine if the woman's CD4+ T-lymphocyte count was less than 250 cells per mm³ [18] or ritonavir-boosted lopinavir if the woman's CD4+ T-lymphocyte count was higher. HAART users with a documented quantitative HIV RNA concentration ("viral load") less than 1,000 viral particles/ml³ were advised to deliver vaginally; non-HAART users and those with unknown or higher viral loads were encouraged to undergo elective cesarean delivery.

2.3. Laboratory Testing. Plasma specimens were obtained at age one to 25 months from known perinatally exposed and/or HIV-antibody-positive infants born from 1999–2005 for DNA polymerase chain reaction (PCR) qualitative or quantitative HIV-1 "viral load" testing. If viral nucleic acid was detected, testing was repeated. If the result was negative and the sample had been obtained prior to six months of age, the test was repeated at age of six months. From 2006–2011, dried blood spots (DBS) obtained from perinatally exposed and/or HIV-antibody-positive infants and children aged one to 25 months were collected according to previously published procedures and tested for viral nucleic acid [19].

2.4. Data Abstraction, Processing and Analysis. Information regarding maternal HIV diagnosis, prenatal antiretroviral treatment, delivery, and infant antiretroviral treatment and nutrition was obtained from maternal and infant medical records from 1999 to 2005. Physicians and nurses providing care for perinatally HIV-exposed infants queried the parents or guardians about this information 2006–2011 and documented their responses on laboratory requisition forms for HIV PCR testing on DBSs when the parent or guardian consented to the infant's HIV PCR test. No attempts were made to verify the data obtained, beyond reviewing maternal or infant records, if available. When guardians did not have the information, and it was not found in requisitions or records, values were coded as missing.

Data were entered into Excel databases, (one in La Romana, and the other for the rest of the sites) and updated with the DBS HIV test results when they were received. In 2012, the Excel databases were converted to Epi Info v3.5.1 for Windows (Centers for Disease Control and Prevention, 2008) files, the variables were harmonized, and the databases were merged and analyzed [20].

HIV MTCT rates per 100 infants and children were calculated for maternal and infant antiretroviral regimen, delivery and infant nutrition characteristics, year and period (pre- and post-HAART for pMTCT guidelines) of birth, and by the various pMTCT strategies. Chi-square or Fisher's exact two-tailed tests were used to evaluate categorical

variables for statistical significance. The Kruskal-Wallis test for two groups was used for continuous variables. Stratified analyses were performed to control for confounding.

2.5. Prenatal and Infant Feeding Practices. Proportions of women who attended prenatal care, had hospital deliveries and breastfed were obtained from 2007 Demographic and Health Survey (DHS) data [12]. Data on HIV in *bateyes* (underserved sugarcane plantation communities) were obtained from a DHS 2007 component [15]. Updates on pMTCT strategies in 2003–2005, 2009, and HIV prevalence estimates, projections, and national prevention objectives in 2009 were reviewed [14, 16, 21].

3. Results

3.1. Population. Data from 1,576 infants and children born from December 1, 1999 to December 31, 2011 were analyzed. These included data collected in 34 centers from 1,274 infants born from 1999–2008, and in 18 centers from 302 infants born from January 1, 2009 to December 31, 2011 (Figure 1). Age at specimen collection ranged from 20 days to 25 months (median = 3.0 months; mean = 4.7; s.d. = 3.9; mode = 2.0 months); 1,541 (97.8%) samples were collected before the child was 15 months old.

3.2. Prenatal, Delivery, and Postpartum pMTCT Practices. From 1999 to 2008, HIV infection was diagnosed during the pregnancy in 48.4% mothers, prior to the pregnancy in 21.7%, and during labor or within 72 hours of birth in 5.7% and 5.2%, respectively (Table 1). Maternal HIV infection was diagnosed after 72 hours and during the child's infancy or early childhood in 12.6%. In 6.3%, testing was performed and maternal HIV infection was diagnosed at other or unknown times. After publication of the national guidelines recommending HAART for pMTCT (2009–2011), the proportion diagnosed during labor and delivery rose and the proportions diagnosed within 72 hours of birth and at other or unknown times declined significantly. Otherwise, the distribution did not change significantly from the 1999 to 2008 period.

Maternal antiretroviral use during pregnancy, labor, or delivery rose significantly (Table 1). Women in the earlier period were significantly more likely to receive a single-dose nevirapine regimen than women who delivered from 2009 to 2011. Conversely, women who delivered from 2009 to 2011 were significantly more likely to receive HAART than in 1999 to 2008. All 157 women who received HAART before 2009 had CD4+ T-lymphocyte counts less than 250 per mm³. The majority (57.6%) of women who delivered in 2009–2011 received HAART, and most of these HAART recipients had CD4 counts higher than 250 and received ritonavir-boosted lopinavir. Duration of nevirapine-containing HAART at delivery (median = 286 days) was longer than the duration of lopinavir-containing HAART (median = 104 days; $P < .001$); mothers who used nevirapine-containing HAART were more likely to have started it before pregnancy than those who used lopinavir-containing HAART. Use of other multidose

TABLE 1: Characteristics of maternal HIV diagnosis, maternal and infant antiretroviral use, mode of delivery and infant feeding, Dominican Republic, 1999–2008, and 2009–2011.

	1999–2008 No. (%) N = 1,274	2009–2011 No. (%) N = 302
Diagnosis and management		
Time of HIV diagnosis		
Before pregnancy	277 (21.7)	77 (25.5)
During pregnancy	617 (48.4)	143 (47.4)
Labor/delivery	73 (5.7)	38 (12.6)*
≤72 hours post-partum	66 (5.2)	5 (1.7)*
After 72 hours	160 (12.6)	38 (12.6)
Unknown	81 (6.3)	1 (0.3)*
Maternal antiretroviral use		
Any	868 (68.1)	265 (87.7)*
HAART, either	157 (12.3)	205 (67.9)*
AZT + 3TC + NVP ¹	157 (12.3)	59 (19.5)
AZT-3TC-Lop ²	—	146 (48.3)*
Multidose AZT	19 (1.5)	0
Multidose AZT + 3TC	61 (4.8)	—
Single dose NVP ³	503 (39.5)	60 (19.5)*
Received no ARVs	406 (31.9)	37 (12.2)*
Unknown	121 (9.5)	0*
Type of delivery		
Vaginal	285 (22.4)	81 (26.8)
All Caesareans	882 (69.2)	199 (65.9)
Elective caesarian	882 (69.2)	152 (50.3)
Emergency caesarean	—	47 (15.6)
Unknown	107 (8.4)	22 (7.3)
Infant nutrition		
Formula only	972 (76.3)	260 (86.1)*
Breast feeding only	67 (5.3)	4 (1.3)*
Both	43 (3.4)	13 (4.2)
Unknown	192 (15.1)	25 (8.3)*
Infant antiretrovirals (ARVs)		
Started between 8–72 hours	782 (61.4)	184 (60.9)
Multidose AZT	81 (6.4)	126 (41.7)*
Single-dose NVP only	701 (55.0)	58 (19.3)*
Did not receive ARVs	219 (17.2)	74 (24.6)*
Unknown	273 (21.4)	44 (14.5)*

* $P < .01$ by time period.¹ Zidovudine, lamivudine, nevirapine highly active antiretroviral therapy.² Zidovudine, lamivudine, ritonavir-boosted lopinavir highly active antiretroviral therapy.

non-HAART regimens for one to 24 weeks was reported in 61 women who received combined zidovudine-lamivudine and 19 who received zidovudine during the pregnancy and caesarean delivery in the period 1999–2008; no multi-dose antiretroviral regimens other than HAART were reported in 2009–2011 (Table 1).

Over 60% of infants in both periods were delivered by caesarean section and were administered antiretrovirals between 8 and 72 hours after birth; these proportions did not vary significantly by period (Table 1). A single dose of nevirapine was administered to most infants who received

antiretrovirals from 1999 to 2008, while most infants in the 2009–2011 period who received antiretrovirals received a multidose regimen ($P < .01$). The proportion who were exclusively formula-fed rose and the proportion who were exclusively breastfed declined significantly.

3.3. Perinatally Acquired HIV Infection. Overall, in both periods combined, HIV infection was diagnosed in 154/1,576 (9.8%) of perinatally exposed infants and children. The proportion infected declined from 11.1% (142/1,274) in 1999–2008 to 4.0% (12/302) in 2009–2011 ($P < .001$)

(Table 2). MTCT varied in both periods by whether or not mothers received any antiretrovirals during pregnancy or delivery, and by type of antiretroviral regimen. MTCT rates were similar for infants whose mothers received single-dose nevirapine, regardless of when the nevirapine was given in 1999–2008. The MTCT rate in infants whose mothers received single-dose nevirapine was higher than in those whose mothers received prenatal HAART in 1999–2008 and in 2009–2011 (6.4% versus 2.5% and 5.7% versus 2.9%, resp.) (Table 2). However, the difference was only statistically significant when the two periods were combined; 9/331 [2.7%]) infants of mothers who received HAART were infected, versus 35/601 (5.8%) infants of mothers who received single-dose nevirapine ($P = .03$).

The MTCT rate among infants of mothers who received HAART varied significantly by how long the mother had received HAART at delivery. HAART duration was shorter (median = 16.5 days) in mothers whose infants were infected than in mothers whose infants were not infected (median = 161 days; $P = .003$). In the 1999–2008 period, MTCT rates varied considerably by type of delivery, ranging from 6.8% with cesarean delivery to 23.9% with vaginal delivery. MTCT rates in the latter period were lower for both types of delivery (2.5% and 7.5% in infants delivered by cesarean and vaginally, resp.). MTCT rates also were higher and tended to vary more by infant-feeding strategy in 1999–2008 than in 2009–2011.

MTCT rates varied from 5.0% and 6.1% among infants receiving six weeks of zidovudine or single-dose nevirapine within 72 hours of birth, respectively, to 9.4% among infants who did not receive any antiretroviral in 1999–2008 (Table 2). In contrast, in 2009–2011, when most infants received antiretrovirals, MTCT rates ranged from 2.4% to 5.6% among infants receiving single-dose nevirapine or six weeks of zidovudine, and the differences were not significant. MTCT rates varied significantly in 1999–2008 from 8.1% in exclusively formula-fed infants to 37.3% in exclusively breastfed infants. In the latter periods, only 6 infants received breast milk; MTCT rate in those who were exclusively formula fed or receiving unknown nutrition was 4.1% and 4.0%, significantly lower than in 1999–2008. When the analysis was confined to infants whose mothers had received HAART, were delivered by cesarean and had exclusive formula feeding, the MTCT rate was 1.6% in 1999–2008 and 2.3% in 2009–2011. Only 1 of 81 infants born in La Romana in 2011 (1.2%) was infected.

MTCT rates varied significantly by center (Table 3); the MTCT rate in the La Romana center was lower than in other centers in both time periods, but the difference was only significant in 1999–2008 ($P < .001$). The decline in MTCT risk from 1999–2008 to 2009–2011 was from a higher baseline, of greater magnitude, and statistically significant at centers outside La Romana. The decline in the La Romana center was not statistically significant. When controlled for prenatal antiretroviral use and exclusive formula feeding, no differences in MTCT rates between La Romana and other centers were significant (Tables 2 and 3). Most of the declines in MTCT and the differences by center (Table 3) were due to higher use of maternal antiretrovirals and exclusive formula

feeding in La Romana in 1999–2008, and higher use of maternal antiretrovirals and exclusive formula feeding in 2009–2011 in all centers.

3.4. Prenatal Screening, Delivery, and Infant Nutrition Practices in the DR. Prenatal care utilization in the DR was estimated at greater than 95% in 2007, and varied from 96.6% in Elias Piña to 99.6% in Santo Domingo and from 95.1% in women who had never attended school (uneducated) to 99.6% among high school graduates [13]. Almost all births (97.8%) of births were attended by a health professional, ranging from 84% in Elias Piña to 99.7% in Santo Domingo, and from 91.0% to 99.7% among uneducated and high school graduates, respectively. The vast majority (97.5%) of births occurred in hospitals (ranging from 83.3% to 99.1% in Elias Piña and Santo Domingo, and from 89.2% to 98.7% among uneducated women and high school graduates, resp.). The mean number of prenatal visits was 6.6. Only 7.8% of infants aged 0–5 months were exclusively breastfed [13]. In 2003–2005, in a survey of sentinel sites, over 95% of women consented to HIV prenatal testing; only 76% received their test results [21]. In one of the largest DR centers, samples for rapid tests are collected, stored, and performed at the end of the day; the pregnant women were asked to return the next day or week for the results [14]. HIV prevalence in pregnant women varied with the highest prevalence in La Vega (8.4%), Mao (5.4%) and La Romana (3.2%) [16].

Residents of *bateyes* (generally underserved persons, many of Haitian origin), were surveyed [15]; 92% of women who had a recent pregnancy had been tested for HIV during the pregnancy, but only 58% received posttest counseling, including their test results. HIV prevalence among female residents in *bateyes* was higher (3.1%) than in the general female DR population (0.8%) and varied from 3.1% among 20–24 year olds to 4.9% among 30–34 year olds, and was highest (7.9%) among women aged 45–49 years old. HIV prevalence in DR women varied by educational attainment, from less than .3% in high school graduates to 3.7% in uneducated women [12, 16]. HIV prevalence in the general population varied geographically, with highest prevalence in the northernmost border with Haiti (1.6%) and the eastern sugar-growing region, where La Romana and most *bateyes* are located (1.2%), and the lowest prevalence in the middle-border region (.4%).

4. Discussion

The data in this study suggest that elimination of MTCT in the DR is feasible and attainable. Encouraging signs include the significant increases in proportion of women who received antiretrovirals during their pregnancy, with most of that increase being in HAART use in women without severe immunodeficiency, and the proportion of infants receiving exclusive formula feeding. These increases coincide with and largely explain the decrease in MTCT observed in the years since the publication of guidelines for use of HAART for pMTCT. They also coincide with some national

TABLE 2: HIV mother-to-child transmission risk in the 1999–2008 and 2009–2011 periods, by prenatal antiretroviral, delivery route, and infant feeding prevention strategies, Dominican Republic.

All perinatally exposed	142/1,274 (11.1%)	12/302 (4.0%)*
Any maternal antiretrovirals	54/861 (6.3)	10/267 (3.7)
HAART ¹ all	4/157 (2.5)	5/174 (2.9)
AZT + 3TC + NVP ²	4/157 (2.5)	0/59
AZT + 3TC + Lopinavir/r ³	—	5/115 (4.3)
Non-HAART multidose	4/80 (5.0)	—
AZT-containing regimen		
Single-dose NVP ALL	32/506 (6.3)	3/60 (5.0)
8 hours precesarean	25/395 (6.3)	0/2
Labor onset	5/78 (6.4)	—
At delivery	2/30 (6.7)	—
Unspecified	—	3/58 (5.2)
Unknown	14/211 (11.6)	2/30 (6.7)
None	88/413 (21.3)[†]	2/35 (5.7)*
Delivery		
Vaginal	68/285 (23.9) [†]	6/80 (7.5)*
Caesarean	60/882 (6.8)	5/199 (2.5)*
Unknown	14/107 (13.1)	1/23 (4.3)*
Infant antiretrovirals		
Single-dose Nevirapine (SD NVP)	48/782 (6.1)	1/41 (2.4)
SD-NVP after 72 hours	1/13 (7.6)	—
Zidovudine for six weeks	7/139 (5.0)	7/126 (5.6)
Unknown/other/none	32/340 (9.4) [†]	4/135 (3.0)
Infant feeding		
Breast fed only	25/67 (37.3)	0/2
Mixed	16/43 (37.2)	0/4
Formula only	79/972 (8.1) [†]	11/271 (4.1)*
Unknown	22/192 (11.5)	1/25 (4.0)*

* $P < .05$, comparison by time period, 1999–2008 versus 2009–2011.

[†] $P < .01$ within period, by strategy.

¹ Highly active antiretroviral therapy.

² AZT-3TC-NVP: zidovudine, lamivudine, nevirapine.

³ AZT-3TC-Lop/r: zidovudine, lamivudine, lopinavir (ritonavir boosted).

trends that suggest a possible decline in HIV prevalence and unsafe sex practices, and documented increase in HAART use nationwide [1, 12, 16, 22, 23].

These encouraging findings contrast with persistent problems implementing the fundamentals of effective pMTCT, particularly informing pregnant women of their HIV status, and linking them to care and HAART. It is clear that all of the components of the “cascade” needed for MTCT elimination are present in the DR. These include high use of prenatal care and institutional delivery by trained personnel; high acceptability of prenatal HIV testing, formula feeding, and prenatal, perinatal, and infant antiretroviral use, and legislation that offers some protection, though modest and with draconian components, for people living with HIV [24, 25].

Yet the “weak links” in this system are unfortunately at points where they threaten the many strengths of the program. The principal weak links include the high proportion of women tested in prenatal care who do not receive their

results. According to national guidelines, prenatal HIV testing in the DR is to be performed using rapid antibody tests; results of samples that test positive are then confirmed with another rapid test that uses a different principle, according to WHO guidelines [26], allowing infected pregnant women to receive at least presumptive, if not confirmed, positive test results in the same visit in which the sample for testing is obtained. Yet according to an observational study and a case report in some centers, samples were stored as they were collected and rapid tests run once a day; women were asked to return for their results, and posttest counseling sometimes consisted of reporting that the test “needs to be repeated” without clarifying that it was a presumptive positive test, leading to women delivering without an HIV diagnosis, MTCT, and maternal and infant HIV progression and death [14, 27, 28].

Another potential weakness in the cascade is the linkage to specialized care for an expedited CD4+ T-lymphocyte count to determine which HAART and other treatments are

TABLE 3: Mother to child transmission (MTCT) rates by period (before recommendation of highly active antiretroviral therapy (HAART) for prevention of MTCT (1999–2008), and after (2009–2011) by center (La Romana center versus others) and prevention strategies, Dominican Republic.

	1999–2008 MTCT rate No. of infected/total (%)	<i>P</i>	2009–2011 MTCT rate No. of infected/total (%)	<i>P</i>
La Romana	20/301 (6.6)	<.001	8/212 (3.8)	.9
Other centers	122/973 (12.5)		4/90 (4.9)*	
Any prenatal antiretroviral use				
La Romana	6/179 (3.3)	.16	8/187 (4.3)	.8
Other centers	34/561 (6.1)		2/78 (2.6)	
Any prenatal antiretroviral use, formula only				
La Romana	6/149 (4.0)	.28	8/183 (4.4)	.7
Other centers	35/547 (6.4)		1/53 (1.9)	
No prenatal antiretroviral use				
La Romana	13/114 (11.4)	.002	0/25 (0)	.036
Other centers	75/299 (25.1)		2/12 (16.7)	
No prenatal antiretroviral use, formula only				
La Romana	4/31 (12.9)	.51	0/25 (0)	.15
Other centers	26/146 (17.8)		2/10 (20)	

* Difference between 1999–2008 period and 2009–2011 period $P < .05$.

indicated for the mother's health and pMTCT. In at least one center, in La Romana, this is facilitated by having the counselor (usually a woman living with HIV herself [21]), contact an HIV comprehensive care unit to have staff from that unit personally meet with and expedite the pregnant woman's linkage to care. Models of this type in the DR have demonstrated the feasibility of effective linkage to care for pMTCT and maternal health. However, in centers whose referral process consists of asking the women to schedule an appointment with a specialized clinic, many women will not receive HAART, even if they continue prenatal care. Moreover, despite a high level of utilization of prenatal care and hospital delivery, the populations least likely to access these services include the most HIV-affected [12, 15]; alternative methods of reaching these populations are essential.

The dependence on ritonavir-boosted lopinavir (instead of efavirenz, as recommended by the WHO [29]) for HAART for women who are not severely immunosuppressed because of probably exaggerated concerns about its teratogenicity may limit their antiretroviral options in the future, and incurs a prohibitive cost compared to efavirenz [6]. Finally, although there is growing acceptance of the rights of people living with HIV, stigma, and discrimination continue to affect women with HIV in the DR [30, 31]. These women may also be unaware of their right to HAART at no cost [24, 25]. In the past, some HIV-infected women who did not receive their results found that they were given instead to employers, landlords or medical personnel; they were denied employment, housing, and elective medical services, including cesarean delivery for pMTCT [30, 31]. The new law criminalizes even protected sex with an uninfected partner;

thus, some DR women who know or suspect their status may consider the risks of testing to be unacceptably high [24].

This study has several strengths. It contains data on by far the largest number of HIV perinatally exposed infants of any study conducted in the DR. A considerable amount of data was collected on infants from a large number of diverse centers distributed widely throughout the country. However, this analysis has several problems that limit its generalizability in characterizing MTCT in the DR. First, surveillance for perinatal HIV exposure that depends on testing living infants and children is susceptible to the important survival bias related to the high mortality (up to 30%) of untreated perinatally acquired HIV infection in the first two years of life [28]. Also, these data do not represent the majority of cases of perinatal exposure in the DR; the estimates of HIV prevalence in some DR pregnant and childbearing populations, and the numbers of HIV-infected women delivering each year (notably in La Romana and some sentinel surveillance hospitals) have been confirmed by several studies [13, 17], enabling reliable estimates of the proportion of perinatally exposed infants that are returned for virologic testing. At the national level, the estimated number of women with HIV who deliver annually (at least 1,400 to over 5,700) is much higher than the number of infants tested. This study represents at best a small proportion of DR perinatally exposed infants [6, 13, 16, 17, 21], and greatly over represents the centers (the NGO in La Romana and one of the public Maternity Hospitals in Santo Domingo) [14] with the best outcomes.

Despite these limitations, this analysis represents the first glimpse of the impact of the historic recommendations for HAART use for pMTCT with a large, representative

database. It suggests that MTCT elimination is possible with current tools; indeed, some of the DR's 2012 benchmarks were achieved in 2011 [16]. Barriers to elimination are related to failures to ensure that HIV-infected women are informed of their status and linked to care. Structural barriers limit healthcare access for the DR's most HIV-affected, most marginalized populations. Surmounting these barriers requires innovative strategies to close the gaps in this promising model [32].

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