



Mother to Child Transmission of Human Immunodeficiency Virus: The Jerusalem Experience, 1996–2006

Uriel Elchalal MD¹, Meytal Avgil MSc¹, Tania Goslitzer MD², Diana Averbuch MD³, Dan Engelhard MD³, Michele Haouzi RN² and Shlomo Maayan MD²

¹Department of Obstetrics and Gynecology, ²AIDS Medicine Unit and ³Department of Pediatrics, Hadassah-Hebrew University Medical Center (Ein Kerem Campus), Jerusalem, Israel

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Abstract

Background: In recent years, mother to child transmission of human immunodeficiency virus in the west has decreased markedly due to the advent of antiretroviral drugs given during pregnancy, cessation of lactation, and careful monitoring of viral load in the perinatal period.

Objective: To assess mother to child transmission of HIV among Ethiopian immigrants and non-Ethiopians in the Jerusalem area.

Methods: We conducted a prospective analysis of all deliveries of HIV-positive women in the Jerusalem district over a 10 year period.

Results: Between 1996 and 2006, 35 HIV⁺ women gave birth to 45 infants. Thirty-one (88%) of these women were of Ethiopian origin and gave birth to 39 infants. Of the 35 HIV⁺ women, 30 were aware of being HIV positive. They gave birth to 40 infants. Another 5 women (14%) were not aware of being HIV⁺ during delivery. They gave birth to five infants. Of the group of known HIV⁺ women, 26 (87%) were Ethiopian immigrants who delivered 34 infants and 4 were non-Ethiopians who delivered 6 infants. In the group of five women not aware of being HIV⁺, all were Ethiopians. Breast-feeding data were available for 32 of the 35 women. Only 2 women (6.2%) breast-fed their babies. Neither was aware of being HIV⁺. In the Ethiopian immigrant group (both known and unknown HIV status), 11 deliveries (28%) were vaginal, 18 (46%) were elective cesarean section and 10 (26%) were delivered by emergency cesarean section. Of the 26 known HIV⁺ Ethiopian women, 3 (12%) refused antiretroviral treatment despite repeated counseling. In the non-Ethiopian group, all deliveries were elective cesarean sections. Mother to child transmission of HIV occurred in 4 of the total 45 deliveries (8.8%). Of the 4 transmission cases, 2 occurred among 40 deliveries of known HIV⁺ women (5%), and 2 occurred among the 5 deliveries of women not aware of being HIV⁺ (40%, $P = 0.05$). In the group of Ethiopian women only, HIV transmission occurred in 4 of 39 deliveries (10%), of which 2 occurred among 34 deliveries (5.8%) of women known to be HIV⁺ and 2 among 5 deliveries (40%) of women not aware of being HIV⁺ ($P = 0.08$).

Conclusions: Pregnant Ethiopian immigrants whose HIV status was known during pregnancy were at relatively high risk of HIV transmission despite the availability of antiretroviral drugs and counseling. This is likely due to inadequate adherence to ART preventive regimens, not dissimilar to the poor adherence observed among other immigrant groups in western countries.

The substantial proportion of women, all Ethiopians, unaware of being HIV⁺ at delivery, together with the significantly higher HIV transmission in that group compared to women who knew their HIV status, call for a revision of the current Ministry of Health opt-in policy for prenatal HIV screening.

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In recent years, mother to child transmission of human immunodeficiency virus has decreased to negligible rates in the developed world. This achievement is related to the advent of antiretroviral treatment and prophylactic regimens to both mothers and newborns [1-4], cessation of lactation [5], and elective cesarean sections [6]. Most perinatal transmissions in HIV-infected women who are not treated by ART occur near or during delivery [7] and are related to the viral load before delivery [1,4,6], time elapsed between fetal membrane rupture and actual delivery [8], and breast-feeding [5]. Using ART during pregnancy and delivery reduces the MTCT rates by 80% [1,9], and adding an elective cesarean section leads to further reduction of MTCT to 1–2% only [9]. In Israel, only one previous study addressed the issue of MTCT of HIV [10]. In that study on Ethiopian women there was one transmission among 41 deliveries (2%), occurring in a non-adherent patient.

According to the Israeli Ministry of Health, during the years 2001–2003 an average of 29 mothers living with AIDS gave birth annually; approximately 90 HIV⁺ children who were infected perinatally and under the age of 12 were living in Israel [11]. Most of these children (75%) were born to mothers originating in countries with a generalized HIV epidemic, mainly Ethiopia.

HIV prevalence among adults in the Ethiopian community in

HIV = human immunodeficiency virus

ART = antiretroviral therapy

MTCT = mother to child transmission

Israel varies between 3% and 6% [12], and 50% of the Israeli HIV caseload of approximately 4000 comprised individuals who had emigrated from areas of generalized HIV epidemic, mainly Ethiopia [13]. All HIV⁺ immigrants are eligible for free ART, as are other HIV⁺ Israelis. The Ministry of Health employs case managers of Ethiopian origin to assist HIV⁺ patients in overcoming problems of adhering to ART. The current HIV screening policy during pregnancy recommends the “opt-in” option, namely, counseling prior to HIV testing, which is offered to all pregnant women in the country. The acceptance rate of this policy is low [14].

In the present study we aimed to explore factors related to MTCT of HIV in the Jerusalem area over a 10 year period. Most HIV⁺ pregnant women were immigrants from Ethiopia.

Patients and Methods

HIV⁺ pregnant women from the Jerusalem district were followed from January 1996 to December 2006. Prenatal follow-up started on the first visit with the offer of ART. In women who were already on highly active ART, therapy was continued and modified appropriately. Women who were diagnosed following the detection of HIV in their children were included in the routine follow-up conducted by the AIDS clinic. The ACTG protocol 076 was offered to all pregnant women not receiving ART [2,3], and several women were given Combivir® instead of zidovudine. Adherence to ART prophylaxis during pregnancy was monitored by the case managers. Monitoring included frequent home visits, during which adherence was emphasized.

HIV viral load was measured at the first visit and at least once during pregnancy. The last VL was taken within a month prior to the expected date of delivery. Elective cesarean section before labor and rupture of the membranes was offered to all consenting women. After delivery, lactation was not allowed. The lactation prohibition was monitored by frequent home visits by case managers. At birth, infants were tested initially by VL (Roche). Further VL tests were performed at 3, 6 and 12 months of age.

HIV-1 serological status was determined by commercial enzyme-linked immunosorbent assay. ELISA tests were also done at birth and at 3, 6 and 12 months. ELISA results were confirmed by western blot analysis. CD4 enumeration was performed by flow cytometry.

Newborn infants who had two or more VL determinations of more than 1000 copies/ml within the first 3 months of life after birth were classified as HIV infected. In children who were detected initially after birth, detection of HIV antibody by ELISA and confirmation by Western blot was required for the definition of HIV infection. Children who were seronegative at 6 and 12 months were considered HIV negative.

Results

Over a 10 year period, a total of 35 HIV⁺ women gave birth to 45 infants (45 mother-child pairs). Of these women, 31 (88%) were Ethiopian immigrants who gave birth to 39 infants and 4 were non-Ethiopians who gave birth to 6 infants. Deliveries in HIV⁺ Ethiopian immigrant women comprised 4% of all 1095

Table 1. Maternal characteristics

	Ethiopian immigrants (n=31)	Non-Ethiopians (n=4)
No. of pregnancies	39	6
Maternal age (yrs) (mean ± SD)	27.6 ± 6.2	29 ± 3.5
Pregnancy order	2.5 ± 1.1	1.3 ± 0.5
Week of delivery (median)	38	38
Mode of delivery		
Vaginal	11	–
Emergency cesarean	10	–
Elective cesarean	18	6
Time from rupture of membranes (min)*	136	–
ART (total no. of pregnancies)	31	6
ACTG protocol	16	2
Combivir	2	
HAART	14	4
No ART	8**	
Newborn weight at delivery (g)	2567 ± 850	3325 ± 100
MTCT	4/39 (10%)	0/6 (0%)

* Mean time elapsed from membrane rupture to delivery.

**Including 5 who were not aware of being HIV positive

deliveries among Ethiopian women in the Jerusalem district during that period. The mean age of HIV⁺ pregnant Ethiopians and non-Ethiopians was 27.6 ± 6.2 and 29 ± 3.4 years respectively. The median gestational age at delivery was very similar, 38 ± 2.8 weeks among Ethiopians and 38 ± 0.8 among non-Ethiopians [Table 1].

Known vs. unknown HIV status

Of the 35 women comprising the cohort, HIV status was known in 30 (85%). Most (n=26) were Ethiopians. These women gave birth to 40 infants. In another 5 women (15%), all Ethiopians, HIV status was not known prior to delivery. They gave birth to five infants.

Treatment and adherence to ART among Ethiopian women

Zidovudine-containing regimens were given in 31 of 39 pregnancies (79%) of Ethiopian immigrant women and in all pregnancies of non-Ethiopians. In 17/31 pregnancies (55%) of immigrant women, zidovudine was given as part of the ACTG protocol 076 [2]. In the others it was given as part of HAART.

Adherence to azidothymidine or ART during pregnancy was judged by counselors and treating staff as adequate in 22/26 (87%) known HIV⁺ Ethiopian women. Of the four non-adherent Ethiopian women (13%), zidovudine was declined in 3.

Viral load and CD4 counts

Viral load in the month prior to delivery was available in 31/34 pregnancies (92%) of known HIV⁺ Ethiopian women among all

VL = viral load

ELISA = enzyme-linked immunosorbent assay

HAART = highly active antiretroviral treatment

pregnancies of non-Ethiopians. Mean VL among 22 Ethiopian women adherent to therapy was 1489 ± 4118 copies/ml (median 400 copies/ml, range 46–21,000 copies/ml). VL of more than 1000 copies/ml was measured in 4 of 29 pregnancies (14%) of these women. VL of 7000 and 22,000 copies/ml, respectively, was available in 2/4 pregnancies of non-adherent women. In the non-Ethiopian HIV⁺ women, mean VL prior to delivery was 278.3 ± 157.5 copies/ml (range 80–400 copies/ml).

CD4 count in the month preceding delivery was available in 30/39 pregnancies (77%) of Ethiopian immigrant women and in 6/6 pregnancies of non-Ethiopians. In the Ethiopian group, the mean CD4 count for adherent women was 410 ± 228 cells/mm³ (range 20–1300 cells/mm³). In two of the four non-adherent women, CD4 count was available: 327 and 612 cells/mm³ respectively. Among non-Ethiopians the mean CD4 count was 382.5 ± 129.6 cells/mm³.

Mode of delivery

The Ethiopian group of 31 women (both known and unknown HIV status) delivered 39 infants. Of these, 11 deliveries (28%) were vaginal, 18 (46%) were elective cesarean section and 10 (26%) were emergency cesarean section. The rates among Ethiopian women with *known* HIV status were 24% vaginal, 53% elective and 23% emergency cesarean section. In the non-Ethiopian group, all deliveries were elective cesarean sections.

Obstetric parameters

Ruptured membranes of more than 4 hours occurred in 1 of 11 vaginal deliveries (9%), and in 3 of 10 (30%) emergency cesarean sections (mean of 141 hours). All occurred in the Ethiopian group.

Breast-feeding

Breast-feeding data were available on 32/35 HIV⁺ women following delivery. Only 2 women (6.2%) breast-fed their babies. Neither was aware of being HIV positive.

HIV transmission (MTCT)

MTCT of HIV occurred in 4 of all 45 deliveries (8.8%). Of the 4 transmission cases, 2 occurred among 40 deliveries of known HIV⁺ women (5%), and 2 occurred among the 5 deliveries of women not aware of being HIV⁺ (40%, $P = 0.05$). These women were tested for HIV following the detection of HIV infection in their infants.

Among Ethiopian women only ($n=31$), MTCT occurred in 4/39 deliveries (10%), of which 2 occurred among 34 deliveries (5.8%) of women known to be HIV⁺ and 2 among 5 deliveries (40%) of women not aware of being HIV⁺ ($P = 0.08$). Regarding the 2/34 MTCT cases, the first occurred in a woman who delivered 3 days following immigration and was not on zidovudine treatment. The second occurred in a woman who was offered HAART during pregnancy but had very poor adherence, and had over 24 hours of premature rupture of membranes. She received intravenous zidovudine during labor, and was delivered by emergency cesarean section due to an obstetric emergency. VL of 14,000 and

22,000 copies/ml respectively were measured in these two women prior to delivery. No case of MTCT occurred in the non-Ethiopian immigrant women.

HIV transmission: deliveries in Ethiopia prior to immigration

Another 27 HIV⁺ immigrant women being followed at the Hadassah AIDS Clinic delivered 38 infants in Ethiopia after 1990 (approximate year of the HIV epidemic spread in Ethiopia) and prior to immigration. They received no prevention of MTCT protocols. HIV transmission occurred in 11/38 infants (29%).

Discussion

In the present study we describe the pregnancy characteristics and outcome in a group of 35 HIV⁺ women who delivered 45 infants in a major city in Israel over a 10 year period. This report focuses on Ethiopian immigrants, who constituted the majority (31/35, 88.5%) of the present HIV⁺ cohort.

The 26 Ethiopian women with known HIV status comprised the majority (26/31, 84%) of Ethiopian women in this cohort. In this group we observed a 5.9% MTCT rate (2/34 deliveries). This rate is lower than the 8% transmission rate observed in the original ACTG 076 paper [2] and lower than the 10% and 8%, respectively, observed in the Ugandan HIVNET 006 and 012 cohort of 642 mother-child pairs (all breast-fed) in which short-course AZT and nevirapine were given perinatally [15,16]. Our MTCT rate is, however, at least twice as high as the 3% and 1% rates, respectively, observed in a more recent European cohort study (4525 mother-child pairs) of the overall transmission rate and that in Western Europe [4].

Our poor/non-adherence rate was 15%. As expected, we observed an association between MTCT and poor adherence. Thus, the two transmission cases occurred among women who did not adhere to ART, resulting in high VL prior to delivery. It is noteworthy, however, that while the VL prior to delivery in the four non-adherent women ranged between 7000 and 22,000 copies/ml, the mean VL measured in the group of 22 adherent women prior to delivery was 1489 copies/ml, suggesting that "adequate adherence" according to our definition was actually sub-optimal. Thus, achieving a viral load of less than 1000 copies/ml to allow for safe vaginal delivery [3,9] cannot be taken for granted in this immigrant group from Ethiopia where sub-optimal adherence is frequent.

Poor, or less than adequate adherence to prolonged therapies is by no way unique to our group of immigrants. Minority groups in the United States were reported to have poor adherence to ART during pregnancy and in the postnatal period [17]. Poor adherence during pregnancy was also observed among immigrant women in Italy given DOT regimens for tuberculosis treatment [18], and Thai immigrant pregnant women in Australia were observed to minimize the use of all medical services in the host country [19]. Thus, immigrant or minority populations in general, and pregnant immigrant in particular, may have difficulties adhering to prolonged medical regimens, and HIV is no exception.

AZT = azidothymidine

Table 2. Detection of HIV infection in 5 women not aware of HIV serostatus during pregnancy and delivery

	Origin	Delivery date	Detection of HIV ⁺ serostatus	HIV transmission to offspring
Case no 1	Ethiopian	9/99	7 days after delivery	No
Case no 2	Ethiopian	12/00	2½ years after delivery	Yes*
Case no 3	Ethiopian	11/01	Few days after delivery	No
Case no 4	Ethiopian	05/02	2 years after delivery	Yes*
Case no 5	Ethiopian	06/03	Week 36	No

* Detection of HIV infection in the child leads to detection of HIV infection in the mother.

In a population with sub-optimal adherence to a preventive MTCT regimen, the role of elective cesarean section should be regarded as an additional safety measure, especially if VL prior to delivery is not known. A recent Cochrane summary of the topic suggests that elective cesarean section will reduce the risk of MTCT in women not taking ART or taking only zidovudine with a measurable VL [20]. Likewise, recent United States Public Health Service data suggest the same, although the recommendations regarding women whose VL on ART is < 1000 are that elective cesarean section may not be necessary [21].

The five Ethiopian women with unknown HIV status at delivery comprised 14% of the total cohort and 16% of the Ethiopian subgroup [Table 2]. In this group, we observed an MTCT rate of 40% (2/5 deliveries), not dissimilar to the 29% rate observed among HIV⁺ women at our clinic who delivered in Ethiopia. The substantial proportion of Ethiopian women in our cohort who were unaware of being HIV⁺ at delivery and the significantly higher HIV transmission in that group compared to women who knew their HIV status pose a question with regard to the adequacy of the current opt-in policy of the Israeli Ministry of Health on prenatal HIV screening [22]. Evidently, the opt-in policy that is currently implemented in Israel, mainly among Ethiopian women, has little impact on HIV testing among these women. Data obtained from the Haifa district public health clinics show that in less than 50% of high risk pregnant women the HIV test had been offered (L. Rubin et al., unpublished). Moreover, it is of interest that since September 2006 the U.S. Centers for Disease Control recommend universal "opt-out" screening for HIV among all pregnant women [23]. That policy has been endorsed by the WHO and UNAIDS [24] and is being implemented in several American states, e.g., New York, New Jersey, Arkansas, in some provinces in Canada, in England, Sweden, France and Holland, and in a growing number of African countries: Botswana, Kenya, Malawi, Uganda, and Zambia [25].

In summary, over a 10 year period, deliveries of HIV⁺ immigrant Ethiopian women constituted a measurable segment (4%) of Ethiopian women delivering in the Jerusalem area. These women were likely to exhibit sub-optimal adherence to preventive MTCT regimens. This led to insufficient suppression of HIV replication prior to delivery and to above-western rates of perinatal HIV

transmission. It appears that this immigrant population needs close supervision and monitoring of adherence to ART during pregnancy. A culturally sensitive approach, preferably by case managers familiar with the Ethiopian community, is necessary to reinforce adherence in this population. Based on our results, elective cesarean section delivery should be considered in all Ethiopian HIV⁺ individuals in order to further reduce HIV transmission. Furthermore, based on our results, a revision of Israel's opt-in policy regarding perinatal HIV screening is necessary. It is time to introduce a universal opt-out policy to prevent women who are unaware of being HIV positive from entering delivery rooms in Israel, with its resultant very high likelihood of HIV transmission to offspring, as shown in this article.

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- Correspondence:** Dr. S. Maayan, Unit of AIDS Medicine, Hadassah-Hebrew University Medical Center (Ein Kerem Campus), P.O. Box 12000, Jerusalem 91000, Israel.
Tel: (972-50) 787-4327
Fax: (972-2) 642-2273
email: shlomo_m@hadassah.org.il