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HIV testing and treatment in the antenatal care setting

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Abstract
Routine linked HIV antenatal screening, with a opt-out, was introduced at the Rotunda in January 1998. This paper reviews the screening and subsequent pregnancy management and outcome in HIV positive women from 1998 to 2006. During this time 225 women (280 pregnancies) were HIV positive and 194 women subsequently delivered at the Rotunda, representing 233 liveborn infants. Overall anti-HIV prevalence was 0.42%, increasing from 0.06% in 1998 to 0.57% in 2006. Of 233 livebirths, 111 (48%) were delivered by spontaneous vaginal delivery (SVD). HIV treatment was started pre-pregnancy in 14 (6 %) pregnancies and antenatally in 208 (90%). The vertical transmission rate in mothers receiving >4 weeks of treatment was 0%. We conclude that routine antenatal HIV screening is effective and significantly benefits the health of mother and child.

Introduction
Mother to child transmission (MTCT) of Human Immunodeficiency Virus (HIV) can occur in utero, during delivery and post partum through breastfeeding. Without antiretroviral treatment (ART), transmission rates vary from 15-40% depending on maternal viral load, duration of ruptured membranes, the presence of sexually transmitted infections, mode of delivery, prematurity and breastfeeding. In developed countries transmission to the infant is almost entirely preventable with a combination of interventions: antiretroviral prophylaxis during pregnancy, intrapartum and to the neonate, elective caesarean section and avoidance of breastfeeding. While initial populations identified as HIV positive and pregnant in developed countries were those linked to injecting drug use (IDU), there have been significant changes in such population over the years. Heterosexual transmission is now the major mode of acquisition of HIV infection among women of childbearing years, representing the fastest increasing group of newly infected individuals.

The Rotunda was the first maternity unit in the Republic of Ireland to introduce routine linked antenatal HIV (antibody) screening, which commenced on 1st January 1998. Prior to this, most identified HIV infection was linked to IDU and selective testing was performed; however it was soon recognised that more universal testing was necessary for optimal identification. Studies carried out elsewhere had also shown that selective testing was inadequate. The introduction of routine testing in Ireland coincided with major demographic changes including significant immigration from sub-Saharan Africa and Eastern Europe. Initially, Zidovudine (ZDV) monotherapy was the standard of care for treatment of such women, but by 2002 Ireland had adopted a strategy of offering triple drug antiretroviral therapy (Highly Active Antiretroviral Therapy, HAART) to all women including women who did not require ART for their own health. This retrospective study audits our experience of routine HIV screening and management of those identified as infected in the first nine years of our programme.

Methods
Demographic, antenatal registration, laboratory, medical history, treatment and delivery data for all HIV positive women from 1998 to 2006 were extracted from the hospital’s patient administration system and patient charts. Infant treatment and outcome was sourced from a national database containing follow-up information for all HIV exposed and infected infants attending the Rainbow clinic, Our Lady’s Children’s Hospital, Crumlin and The Children’s University Hospital, Temple Street. Positive status was assigned where a HIV PCR positive result was obtained on two separate specimens (excluding cord blood). Negative status was assigned where there were at least two negative tests from separate specimens, both of which were performed in an infant who is not receiving ART, at greater than or equal to 1 month of age, and one of which was performed at greater than or equal to 4 months of age. Data were analysed using SPSS v14.0.

Results
In the 9-year audit, 66,598 women booked for antenatal care and 66,585 gave consent (99.98%) for HIV antibody testing. There were 280 pregnancies in 225 HIV positive women; 191 women delivered 227 single liveborn infants and 3 delivered twins. In total there were 230 live births at the Rotunda, 28 transferred to another maternity service and 20 ended in miscarriage in the first/second trimester. Two resulted in a stillbirth, one an intrauterine death at 40 weeks gestation and the other was born before arrival at the hospital (BBA) at 26 weeks.

Figure 1: Number and nationality of HIV positive women booking for antenatal care at the Rotunda Hospital, 1998-2006 (n=280)

Trends and patient characteristics over time
From the initial 4 HIV infected women who booked for antenatal care in 1998, there has been a steady increase and now plateau in the number of HIV positive women booking for antenatal care, with a peak of 58 women in 2003 (Figure 1). While in the early years many of the women identified as HIV and pregnant were Irish with a history of IDU, recent trends in immigration are reflected in the fact that now the majority of women are from Africa. The most prevalent nationalities in this cohort were Nigerian (36%), South African (18%) and Irish (16%). Nine Irish women had two pregnancies, while 34 non-Irish had 2 or more pregnancies in the 9-year period. Women’s median age at first booking visit for each pregnancy (n=280) was 28 years (16-41).

Knowledge of HIV status
Over the 9-year period, 54% (n=150) of pregnancies were in women who were diagnosed with HIV as a result of antenatal screening. Whereas 72% of women were newly diagnosed at antenatal screening in 2003 this has declined to 29% in 2006 (Figure 2). Overall, fewer pregnancies in Irish women (n=12) were newly diagnosed during pregnancy than in non-Irish women (n=138) (Pearson’s 2 test: 16.717, p<0.001)

Figure 2: Knowledge of HIV status in 280 pregnancies at the Rotunda, 1998-2006

Gestation at Booking
The mean gestation at first antenatal visit was 23.8 weeks (+/- 9.8), and the median was 15 weeks (6-42 weeks). There was a significant difference in the gestation at booking of Irish and non-Irish women (Pearson’s 2 test: 7.945; p=0.005). 96% of women booking at ≥36 weeks were non-Irish.

Figure 3: HAART administered in pregnancies resulting in livebirths (n=222), 1998-2006

Treatment over time
Of the 230 pregnancies resulting in livebirths, 222 received ART, 14 of whom had commenced ART prior to pregnancy. Seven women did not receive any/adequate ART due to late booking (booking <24 to 48 hours before delivery) and one woman had a opted-out of HIV screening antenatally. Treatment with triple therapy increased over time (Figure 3) and median duration of ART was 12 weeks (1-42). Overall 44 pregnancies (20.1%) received four or less weeks of treatment (Table 1).

Mode of delivery
111(48%) and 109 (47%) of the 233 live born infants over the 9-year period were born by spontaneous vaginal delivery (SVD) and C-section respectively (Table 1). 19% of emergency Caesarean sections were attributed to late booking (insufficient time on ART), 12% to Hepatitis C and HIV co-infection and the remainder were due to obstetrical reasons, such as malpresentation, failure to advance, previous elective Caesarean section etc. 77% of mothers who received 4 or less weeks of treatment during pregnancy were delivered by Caesarean section. 48% of infants born to mothers receiving ART had a SVD. Of these 59% had a delivery viral load (VL) of <50 copies/mL (cpm).

* Other includes assisted breech, forceps, ventouse and BBA

Viral load and CD4 at delivery

The median viral load taken closest to delivery for the 230 pregnancies resulting in livebirths was 50 cpm (<50-246359). 54% had a viral load of <50cpm, 30% between 50 to 1000 cpm and 12% >1000 cpm. Information was not available for 4% of pregnancies. The median of CD4 cell counts taken closest to delivery was 397.5 cells/mm3. 14% had a CD4 cell counts of <200 cells/mm3, 24% between 200-350 cells/mm3, 23% between 351-500 cells/mm3 and 30% had a CD4 cell count of >500 cells/mm3 (counts were unknown for 8% of pregnancies).

ZDV during labour

ZDV was administered intrapartum in 215 pregnancies, regardless of prior use in the current or previous pregnancy (standard dosage used was 2mg/kg loading dose over 1 hour followed by 1mg/kg/hr until delivery). The median duration of IV-ZDV infusion was 4 hours 45 minutes (5 minutes - 45 hours and 30 minutes); duration was not known in 52 pregnancies (23%).

Co-infections in pregnancy

Twenty seven women were identified as Hepatitis C antibody positive (25 Irish, 2 African); 23/25 of the Irish women had a history of IDU. Hepatitis B (surface antigen) was identified in 6 African and 1 Irish woman. In addition 19 women of African origin had positive syphilis serology. All co-infections were treated according to standard care practices.

Infant outcome

Of 233 infants delivered, 3 were positive for HIV infection, all of whose mothers had received triple therapy administered late in pregnancy (<4 weeks). One infant was PCR positive at birth while the remaining 2 infants tested positive at 6 weeks.

Maternal Outcome

Of the 225 women in this study there was one maternal death; a case of Nevirapine related liver failure and post-partum death that has been previously reported.¹⁴

Discussion

Unlinked (anonymous) HIV testing was introduced at the Rotunda in July 1991. From 1998 routine linked antenatal HIV screening was introduced, for several reasons. Firstly, it was known from the unlinked screening program that the number of HIV positive women booking as antenatal patients had increased steadily since its introduction. the advent of successful interventions in the reduction of vertical transmission of HIV made it imperative that HIV positive women be identified in pregnancy. The remarkably high uptake of HIV screening tests in our antenatal population reflects the hospital's approach to this potentially sensitive issue. The 'opt-out' system employed prevents any subjective selection of perceived 'high-risk' patients by the midwifery staff. Such selective testing is unreliable as a method of screening, identifying only 8-58% of those who are HIV positive.^{3,16} The 'opt-out' system is also more acceptable to patients as it eliminates any misconception of bias.

¹⁵ Secondly,

The changing trends in the HIV positive women over the years of this audit are interesting. Previously HIV in pregnant women was almost exclusively a problem of IDU. While this persists at a fairly constant level, the major increase has been in the immigrant population, predominantly representing women from Africa. The peak number of HIV positive women observed in 2003 coincides with large scale immigration to Ireland possibly due to changes in immigration and employment legislation that year (Figure 1). Since then the numbers have declined slightly; reaching a plateau in recent years, again in line with national immigration trends. Hepatitis C was the most common co-infection in the cohort; affecting mainly Irish women with a history of IDU. Of note Hepatitis B and/or syphilis co-infections were identified in a number of women of African origin. As these women often present late in pregnancy, treatment times/options are subsequently limited. Also noted over time is the shift in the relative proportion of those for whom a first diagnosis of HIV infection is made during pregnancy. While this is encouraging, suggesting a greater awareness of the benefits of HIV testing in general, the persistence of a significant minority for whom antenatal testing represents their initial diagnosis, highlights the need for continuation of antenatal screening programmes and argues strongly against complacency in this regard.

The ready availability of HAART to all HIV positive pregnant women coupled with close monitoring of viral load in the last trimester of pregnancy has resulted in a C-section delivery in only 47% of 233 livebirths. This is a lower rate than that noted by some centres in the UK, where ZDV monotherapy and elective C-section are still being utilised. However in order to fully evaluate the merits of HAART, future studies will need to examine data on pregnancy outcomes such as gestational diabetes, pre-eclampsia, pre-term delivery, toxicity and drug resistance. Since the introduction of linked antenatal HIV screening in the Rotunda Hospital, there have been three instances of vertical transmission of HIV. These women were known to be HIV infected and chose not to access care, or were newly infected in pregnancy. Such transmissions are avoidable and highlight the need for individualised care, analysis of the factors contributing to these infections and reassessment of interventions to prevent such occurrences. Despite the many barriers to treatment, as a rule, women who are identified in the Irish situation are provided with the standard of care HIV treatments (with a change from monotherapy to dual therapy to triple therapy noted over the study period) and most of the women (98%) who present to labour and delivery have been in receipt of IV ZDV as a direct result of pre-pregnancy or pre-natal HIV screening at some point in time. The 0% MTCT rate observed in our study in women receiving >4 weeks of ARV therapy underlines the benefits of linked HIV screening as a part of routine antenatal care.

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Comments:
