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SHORT COMMUNICATION

Pregnancy outcomes in adolescents in the UK and Ireland growing up with HIV

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Objectives

Adolescents with HIV infection acquired perinatally or in early childhood are becoming sexually active, but little is known about fertility and pregnancy outcomes. Multicentre data on pregnancy outcomes in this population are described here.

Methods

A retrospective case note review of pregnant women with perinatal/early acquired HIV infection, conceiving before 1 September 2009 and attending participating centres in the UK and Ireland, was carried out.

Results

Among 252 women with perinatal/early acquired infection aged 12 years and older under follow-up in 21 centres, 42 pregnancies were reported in 30 women (19 women with a single pregnancy, 10 women with two pregnancies, and one woman with three pregnancies). Fifteen women (50%) had previous AIDS-defining diagnoses. The median age at first reported pregnancy was 18 years (range 14–22 years). Of the 42 pregnancies, 34 (81%) were reportedly unplanned, 31 (74%) involved regular partners, and in 21 (50%) of the 42 pregnancies the partners were reported to be unaware of maternal HIV status. Fifteen of the 42 pregnancies (36%) were electively terminated, six of the 42 (14%) resulted in first-trimester miscarriages and 21 of the 42 (50%) resulted in live births. Maternal viral load was detectable close to delivery in seven of 21 pregnancies (33%). Four infants required neonatal intensive care, three of whom were delivered preterm. One infant is HIV infected, there are ongoing concerns about the development of three of 21 infants (14%), and two of 21 (10%) have been fostered.

Conclusions

Despite access to ongoing sexual health and contraceptive services, unplanned pregnancies are occurring in young women growing up with HIV. Pregnancy care and prevention of onward transmission require complex case management for this emerging population.

Keywords: HIV infection, pregnancy, teenagers

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Introduction

Where combination antiretroviral therapy (cART) is available, perinatally acquired HIV infection has become a chronic disease of childhood [1]. High uptake of antenatal testing, interventions to reduce mother-to-child transmission (MTCT), improved survival, and later age at presentation among children born abroad mean that the average age of perinatally infected children in many European cohorts is now over 12 years [2]. These adolescents are facing the complex task of negotiating sexual relationships with a disease that is transmissible both to partners and to future offspring [3].

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Reproductive health, contraceptive use and pregnancy outcomes have been extensively studied in horizontally infected women, but less is known about the reproductive health of perinatally infected women. The long-term outcomes for babies born to mothers who have lived with HIV throughout puberty, growth and development, with extensive exposure to antiretroviral therapy (ART), are not yet well understood.

Patients and methods

Study population

Health professionals in 21 centres in England, Wales and Ireland, caring for young women infected with HIV either perinatally or in early childhood, contributed data via the HIV in Young People Network (www.hypnet.org.uk), a multidisciplinary network of health professionals and voluntary sector representatives working with young people living with HIV infection. Clinicians were asked to report the number of young women aged 12 years and over with presumed perinatal/early acquired HIV infection cared for in their centre, and how many reported pregnancies before September 2009. For each young woman who had been pregnant, a structured proforma was completed by case note review. Viral loads (VLs) and CD4 cell counts closest to the times of conception and delivery were requested. Data were entered into an Excel spreadsheet and descriptive analyses undertaken.

An adolescent was considered to have perinatally acquired HIV infection if her own mother had presumed or confirmed HIV infection and she was diagnosed at under the age of 16 years in the absence of other risk factors. Reports were compared with national surveillance data reported to the National Study of HIV in Pregnancy and Childhood (NSHPC; methods available at www.nshpc.ucl.ac.uk and [4]).

Results

Two hundred and fifty-two women with presumed perinatal or early acquired infection aged 12 years or older were under follow-up in 21 participating centres in England, Ireland and Wales; 42 pregnancies were reported in 30 women between 1 January 2003 and 1 September 2009, all of whom were aware of their HIV status prior to conception. Twenty-five women were presumed to be perinatally infected and five acquired infection from blood or blood product transfusions before their 10th birthday. Maternal characteristics are shown in Table 1: 70% were of Black African ethnicity, the median age at first reported conception was 18 years (range 14–22 years), and 15 women (50%) had previous AIDS-defining diagnoses. Among 24 women with known resistance patterns, 12 had wild-type virus while five had single and seven dual or triple class resistance. Twenty women (67%) had social service involvement. Eight women (27%) had a previous or current mental health diagnosis that included one or more of major depression, repeated self harm and psychosis.

Table 1 Maternal and pregnancy characteristics

	Number (%) or median [range]
Maternal characteristics ($n = 30$)	
Ethnicity	
Black African	21 (70)
Black other	2 (7)
Caucasian	6 (20)
Mixed race	1 (3)
Previous AIDS diagnosis	15 (50)
Number of previous ART regimens	
0	6 (20)
1–2	9 (30)
3–5	7 (23)
≥ 6	7 (23)
Not known	1 (3)
Age at first conception (years)	18 [14–22]
Pregnancy characteristics ($n = 42$)	
On combination ART at conception	23 (55)
CD4 count at conception	
< 200 cells/μL	16 (38)
200–349 cells/μL	15 (36)
> 350 cells/μL	8 (19)
Not known	3 (7)
Viral load at conception	
< 50 copies/mL	9 (21)
50–999 copies/mL	5 (12)
1000–9999 copies/mL	7 (17)
≥ 10 000 copies/mL	18 (43)
Not known	3 (7)
Outcome of pregnancy	
Termination	15 (36)
First-trimester miscarriage	6 (14)
Live birth	21 (50)

ART, antiretroviral therapy.

Eight pregnancies (19%) were planned, 31 of 42 (74%) involved regular partners, and partners were reported to be aware of the woman's HIV status in 21 of 42 pregnancies (50%). Women were on cART at conception in 23 of 42 pregnancies (55%), at which time five had a CD4 count < 200 cells/μL. Where women were not on cART at conception, CD4 counts were < 200 cells/μL in 11 of 19 pregnancies (58%). Overall, the median CD4 count closest to conception was 244 cells/μL (range 0–837 cells/μL), and the median VL was 18000 HIV-1 RNA copies/mL (range < 50–208 296 copies/mL). Fifteen pregnancies (36%) were electively terminated, six (14%) resulted in first-trimester miscarriages and 21 (50%) resulted in live births.

Table 2 Characteristics of the 17 women with continuing pregnancies

Number	cART at conception	Drug class resistance*	CD4 count at conception (cells/μL)	CD4 count at delivery (cells/μL)	Viral load at conception (copies/mL)	Viral load at delivery (copies/mL)	cART adherence in pregnancy	Delivery	Preterm	SGA	HIV status of baby
1	N	2	<200	<200	≥10 000	50–999	Poor	ELCS	Y	N	Negative
2	N	0	<200	<200	≥10 000	<50	Poor	EMCS	Y	N	Negative
3	N	1	<200	<200	1000–9999	NK	Poor	ELCS	N	N	Negative
4	Y	0	>349	>349	<50	<50	Good	VD	N	N	Negative
5	N	0	<200	<200	≥10 000	>10 000	Poor	ELCS	N	N	Negative
6	Y	3	200–349	200–349	≥10 000	50–999	Good	ELCS	N	Y	Negative
7	Y	0	200–349	<200	<50	50–999	Poor	ELCS	N	N	Negative
8	N	0	200–349	>349	1000–9999	<50	Good	EMCS	Y	N	Negative
9	N	0	200–349	>349	≥10 000	<50	Poor	EMCS	N	N	Negative
10	Y	3	200–349	>349	≥10 000	<50	Poor	ELCS	N	Y	Negative
11	N	1	200–349	200–349	≥10 000	<40	Good	ELCS	N	N	Negative
12	Y	1	<200	<200	≥10 000	50–999	Poor	ELCS	N	N	Infected
13	N	NK	<200	200–349	≥10 000	<50	Good	ELCS	N	N	Negative
14a	Y	2	200–349	>349	50–999	<50	Good	ELCS	N	N	Negative
14b	Y	2	>349	NK	50–999	<50	Good	EMCS	N	N	Negative
15a	Y	2	<200	<200	50–999	50–999	Poor	ELCS	N	N	Negative
15b	Y	2	<200	200–349	1000–9999	<50	Good	ELCS	N	N	PN
16a	N	1	200–349	200–349	≥10 000	50–999	Poor	VD	N	N	Negative
16b	Y	1	>349	>349	<50	<50	Good	VD	N	N	Negative
17a	N	0	200–349	200–349	<50	<50	Good	VD	N	N	Negative
17b	N	0	<200	<200	1000–9999	<50	Good	VD	N	N	Negative

cART, combined antiretroviral therapy; ELCS, elective caesarean section; EMCS, emergency caesarean section (after onset of labour); N, no; NK, not known; PN, presumed negative [initial polymerase chain reaction (PCR) negative but PCR results after 3 months of age or 18-month antibody result not available]; SGA, small for gestational age; VD, vaginal delivery; Y, yes.
*Drug class resistance is the reported cumulative resistance to major antiretroviral drug classes.

The features of the pregnancies leading to live births are summarized in Table 2. Seventeen women had 21 infants (all singletons). In all cases, women were on cART at delivery, with a median CD4 count of 263 cells/μL (range 54–1200 cells/μL), and a median VL of 154 copies/mL (range < 50–39 400 copies/mL). In 13 of 20 pregnancies (65%), women delivered with a VL < 50 copies/mL, but one had a VL > 10 000 copies/mL. Twelve infants were delivered by elective and four by emergency caesarean section. Five infants were delivered vaginally, including one whose mother had detectable virus.

Four infants required neonatal intensive care, including three (14%) who were delivered at 32–36 weeks of gestation. One infant was infected: HIV DNA polymerase chain reaction (PCR) was positive on the day of birth, indicating *in utero* transmission. Although the infant's mother was on cART prior to conception, poor adherence was reported; maternal VL exceeded 22 000 copies/mL around the time of conception and, although reduced, was still detectable at delivery; CD4 count remained < 200 cells/μL throughout pregnancy. The infant was delivered by elective caesarean section at term, received triple cART as post-exposure prophylaxis and quadruple therapy when infection was confirmed. Nineteen of the remaining 20 infants (95%) were HIV DNA PCR negative at 3 months of age or older, and data are missing for one baby. No congenital anomalies were reported. There are concerns about the development of three children: two with speech delay and one who is failing to thrive. Two children are known to have been fostered.

All 30 young women included in this study had been independently notified through routine systems to the NSHPC. Twenty-seven were reported as paediatric cases (eight born in the British Isles and 19 born abroad) and three (all born abroad) when pregnant at 16 years or older. All 21 live births had also been notified to the NSHPC, but 15 of the 21 miscarriages and terminations had not.

Discussion

In the UK and Ireland, young women infected with HIV perinatally or in early childhood are now becoming sexually active and having children of their own. This cohort shares common characteristics with small cohorts of perinatally infected pregnant young women reported from Europe [5], the USA [6,7], Puerto Rico [6] and India [7]; these include significant rates of unplanned pregnancy, low rates of MTCT despite archived resistance mutations limiting treatment options, inconsistent adherence to cART complicating management in pregnancy, and complex social circumstances.

Conception and provision of contraception

Among the young women aged 12 years and over receiving care in 21 participating clinics, 12% were known to have had at least one pregnancy, with a 14% first-trimester miscarriage rate, lower than the 24% reported in horizontally infected women [8], although this could be an underestimate as a result of likely under-reporting of early pregnancy loss. In the USA, which has the largest published cohort of 638 perinatally infected young women, the cumulative incidence of first pregnancy by 19 years of age was 17.2% [95% confidence interval (CI) 11.1, 23.2], substantially lower than first-time pregnancy rates in US girls of a similar age who were presumed to be HIV uninfected (33.5 per 1000 person-years *vs.* 86.7 per 1000 person-years, respectively). The authors speculated that this might be attributable to increased contraceptive availability and awareness, or reduced fertility, in HIV-infected adolescents compared with the general population. They reported that sexually active girls had a higher VL and a lower CD4 percentage and were less likely to be on cART than those who were not sexually active [9].

In a recently reported cohort study of 67 pregnancies in 58 predominantly horizontally infected UK teenagers (median age at conception 18 years), 82% of pregnancies were unplanned, 58% delivered with undetectable virus and one infant was infected. Two-thirds of this cohort were newly diagnosed with HIV during antenatal screening, and therefore had not had prior access to HIV-related sexual and reproductive health support. Despite subsequent access to clinical care and contraceptive services, almost a quarter were pregnant again within 1 year and post termination/delivery contraceptive use was suboptimal [10]. Disappointingly, comparable rates of unplanned pregnancy (81%) were reported in our cohort, despite the fact that most of these perinatally infected young women were in healthcare follow-up with access to enhanced sexual health education and contraception throughout adolescence.

The median age at transition to adult HIV services in the UK is 17 years [3]; these pregnancies were reported both from paediatric settings and following transition to adult services, with the median age at first pregnancy being 18 years. In three-quarters of the pregnancies women were reported to have detectable virus close to conception, with potential associated risk of transmission to partners; only half of the partners were reported by healthcare professionals to be aware of the woman's status up to the time of delivery. While poor uptake of contraception and difficulties with partner disclosure are not limited to adolescence, professionals may need to reconsider their approach to educating this cohort about contraception and partner disclosure, and consider recommending effective long-acting reversible contraception in this population. While barrier contraception is required to reduce the risk of HIV transmission to sexual partners, use is often inconsistent and concentrating on promoting condom use may detract from offering other more effective methods of contraception.

Pregnancy outcomes

Adherence to therapy was reported to be suboptimal at some stage in about half the pregnancies described, with at least one woman requiring hospital admission for directly observed therapy. Problems with attendance and adherence are common during adolescence for many chronic childhood conditions and result in increased disease-related morbidity and mortality [3,11]. Adolescents living with HIV have poorer adherence to cART compared with children or older adult populations, and poor adherence has also been associated with depression, alcohol and substance abuse, and lack of wider disclosure of HIV status [11,12]. cART is effective in preventing first-generation MTCT of HIV with overall MTCT rates < 1% with optimal care [13]. In this cohort a single infant was infected, comparable to other reported adolescent cohorts in the USA (one of 30) [9] and a predominantly horizontally infected UK cohort (one of 66) [10]. Five young women delivered with detectable virus, increasing the risk of transmission to their babies. Multidisciplinary care with the aim of improving adherence to cART during adolescence and particularly during pregnancy should remain a priority; complex social circumstances with frequent social service involvement and high rates of mental health illness should be considered when planning adherence interventions.

The rate of preterm deliveries (14%) in this cohort was almost twice the overall European rate in adolescents [14,15] but similar to the overall rate reported for HIV-positive women in the UK and Ireland [4].

Data are currently sparse on the prevalence of congenital abnormalities in the offspring of perinatally infected adolescents. The initial results of follow-up of antiretroviral-exposed, HIV-uninfected infants born to HIV-positive women appear to be reassuring, with no increase in congenital abnormalities or developmental concerns noted [16,17]. However, perinatally infected women have been exposed to ART throughout much of their postnatal growth and development. Mitochondrial dysfunction in uninfected infants exposed to ART in foetal life has been reported and, as mitochondria are solely maternally inherited, ongoing surveillance of the second generation is needed [16].

It was reassuring that all the births identified by the participating units in this study had also been independently reported to the NSHPC, and were in most cases linked

to the mothers' own paediatric records. However, long-term follow-up is likely to prove challenging as previous attempts to maintain follow-up of children with *in utero* exposure to ART experienced difficulties in enrolment and retention [17].

Conclusions

Appropriate support for perinatally infected adolescents requires significant input from the multidisciplinary team to maintain good health and prevent onward transmission of infection to the patients' sexual partners and offspring. Education around relationships, sexual health and contraception needs to start early in the paediatric clinic in language appropriate to the age and neurocognitive ability of the child and be readdressed during transition and following transfer to adult services. Appropriate adolescent-friendly services that focus on their complex needs are required. Where paediatric healthcare professionals do not have the sexual health expertise required, provision should be made through close liaison with adult sexual health providers.

Timely monitoring of the management and outcome of pregnancies in women with perinatal/early acquired HIV infection is necessary, and should be possible through the established paediatric and obstetric surveillance systems. However, monitoring of the overall fertility and sexual health of perinatally infected young women and men and the well-being of their uninfected children will be much more challenging, and is likely to require more intensive follow-up of perinatally infected adults and their offspring.

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