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Vertical transmission rates for HIV in the British Isles: estimates based on surveillance data

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Abstract

Objective To estimate and interpret time trends in vertical transmission rates for HIV using data from national obstetric and paediatric surveillance registers.

Design Prospective study of HIV infected women reported through obstetric surveillance. HIV infection status of the child and onset of AIDS were reported through paediatric surveillance. Rates of vertical transmission and progression to AIDS rate were estimated by methods that take account of incomplete follow up of children with indeterminate infection status and delay in AIDS reporting.

Setting British Isles.

Subjects Pregnant women infected with HIV whose infection was diagnosed before delivery, and their babies.

Main outcome measures Mother to child transmission of infection and progression to AIDS in children.

Results By January 1999, 800 children born to diagnosed HIV infected women who had not breast fed had been reported. Vertical transmission rates rose to 19.6% (95% confidence interval 8.0% to 32.5%) in 1993 before falling to 2.2% (0% to 7.8%) in 1998. Between 1995 and 1998 use of antiretroviral treatment increased significantly each year, reaching 97% of live births in 1998. The rate of elective caesarean section remained constant, at around 40%, up to 1997 but increased to 62% in 1998. Caesarean section and antiretroviral treatment together were estimated to reduce risk of transmission from 31.6% (13.6% to 52.2%) to 4.2% (0.8% to 8.5%). The proportion of infected children developing AIDS in the first 6 months fell from 17.7% (6.8% to 30.8%) before 1994 to 7.2% (0% to 15.7%) after, coinciding with increased use of prophylaxis against *Pneumocystis carinii* pneumonia.

Conclusions In the British Isles both HIV related morbidity and vertical transmission are being reduced through increased use of interventions.

Introduction

Randomised controlled trials have established that zidovudine can significantly reduce the risk of vertical transmission of HIV.¹ The protective effect of elective caesarean section has been confirmed by a recent meta-analysis of cohort studies² and a randomised controlled trial.³ The combined effect of these interventions is reported to reduce transmission to 2% or less in some cohort studies.^{2,4}

However, the general population of infected women may differ from those recruited into trials or cohort studies in terms of adherence to antiretroviral treatment, previous exposure to antiretroviral treatment, and uptake of elective caesarean section. It is therefore essential to monitor uptake of interventions and vertical transmission rates in the wider population. Here we present estimates of HIV vertical transmission rates in the British Isles.⁵

Methods

Population studied

Since 1989 pregnant women in the British Isles known to be infected with HIV have been notified to the Royal College of Obstetricians and Gynaecologists. Obstetricians are asked to report on outcome of pregnancy and, since 1995, on mode of delivery and uptake of antiretroviral treatment. After initial notification of children born to infected mothers to the British paediatric surveillance unit, paediatricians are asked for diagnostic and clinical data. Subsequently, children of indeterminate infection status are followed until infection status is known.⁵ All reporting is voluntary and confidential. This analysis is confined to prospectively ascertained children whose mothers' HIV infection was reported to have been diagnosed before delivery.

Statistical methods

Statistical methods to avoid biased estimation of vertical transmission rates due to incomplete follow up of

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indeterminates⁶ were adapted and extended. These involve estimating the probability of infection for each indeterminate child based on when they were last known to be seropositive and the fact that they have not yet been reported to have AIDS. The method takes account of AIDS incubation time, delay in AIDS reporting, and time to antibody loss in uninfected children. It was assumed that progression to AIDS in the first six months would have been reduced since 1994 because prophylaxis against *Pneumocystis carinii* pneumonia became routine at that time following UK and US guidelines.⁷⁻⁸

The estimation-maximisation algorithm was used to estimate yearly vertical transmission rates since 1984, and the effect of mode of delivery and antiretroviral treatment during 1995 to 1998. Confidence intervals were estimated by bootstrap sampling from the data (n = 999).⁹ Assumptions on date when *P carinii* prophylaxis became routine and on distribution of delay in AIDS reporting were subjected to sensitivity analysis.

Table 1 Infection status of infants born to diagnosed, HIV infected women between 1984 and 1998 who were not reported to have been breast fed, and vertical transmission rates estimated with estimation-maximisation algorithm

Year of birth	Total live births	Infection status			Estimated vertical transmission rate (95% CI)
		Negative	Positive (AIDS)	Indeterminate	
1984	3	1	1 (0)	1	
1985	17	10	3 (2)	4	9.6* (2.1 to 18.7)
1986	36	31	1 (0)	4	
1987	38	30	2 (2)	6	5.7 (0 to 14.2)
1988	38	29	6 (4)	3	16.5 (5.5 to 29.7)
1989	41	32	3 (1)	6	8.0 (0 to 17.6)
1990	41	27	6 (4)	8	16.6 (5.4 to 29.3)
1991	53	36	4 (2)	13	8.9 (0 to 18.1)
1992	55	38	5 (1)	12	10.6 (2.2 to 19.8)
1993	52	28	8 (2)	16	19.6 (8.0 to 32.5)
1994	69	38	10 (1)	21	19.3 (9.7 to 30.5)
1995	61	36	9 (1)	16	18.9 (8.4 to 30.8)
1996	91	58	10 (3)	23	14.1 (6.4 to 22.5)
1997	85	52	4 (0)	29	6.8 (1.6 to 14.7)
1998	120	42	1 (0)	77	2.2 (0 to 7.8)
Total	800	488	73 (23)	239	12.1 (9.7 to 14.7)

*1984-6 estimate pooled, due to small numbers.

Table 2 Trends in mode of delivery and use of antiretroviral treatment 1995-8

Year of birth	% (No) of elective caesarean sections	% (No) receiving antiretroviral drugs	% (No) receiving >1 antiretroviral drug	% (No) receiving all 3 components of treatment*
1995	42 (24/58)	66 (40/61)	0 (0/39)	54 (15/28)
1996	38 (32/85)	77 (66/86)	3 (1/36)	85 (50/59)
1997	42 (35/84)	84 (70/83)	26 (18/70)	86 (54/63)
1998	62 (74/119)	97 (115/119)	57 (66/116)	89 (93/104)

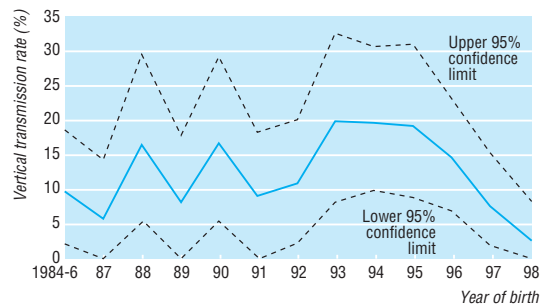
*Antenatal, during labour, and post partum to baby.

Table 3 Effects of elective caesarean section and antiretroviral treatment on vertical transmission rates of HIV, 1995-8 from logistic regression

	Vaginal/emergency caesarean section	Elective caesarean section	Adjusted odds ratio (95% CI)
No antiretroviral treatment	31.6 (13.6 to 52.2)	15.3 (3.4 to 32.7)	1
Antiretroviral treatment	10.1 (4.6 to 16.4)	4.2 (0.8 to 8.5)	0.24 (0.08 to 0.76)*
Adjusted odds ratio (95% CI)	1	0.39 (0.08 to 1.04)†	

* $\chi^2_1=6.9$, P=0.009.

† $\chi^2_1=3.3$, P=0.07.



Year on year estimates of vertical transmission rates and 95% confidence intervals for HIV among children born to mothers known to be infected with HIV and who did not breast feed

Results

By the end of January 1999, a total of 800 prospectively ascertained non-breast fed children born to HIV infected women between 1984 and 1998 had been reported (table 1).

The overall estimation-maximisation algorithm estimate for vertical transmission, which removes the bias caused by indeterminate children, is 12.1% (9.7% to 14.7%). The transmission rate rose to 19.6% (8.0% to 32.5%) in 1993 and from 1995 decreased steeply to 2.2% (0% to 7.8%) in 1998 (figure). The decline in transmission rate from 1995 onwards was significant (odds ratio of 0.51 a year; 95% confidence interval 0.27 to 0.77, $\chi^2_2 = 8.8$, P = 0.003).

Infected children progressed to AIDS within the first 6 months of life at an estimated baseline rate of 17.7% (6.8% to 30.8%) before 1994 and 7.2% (0% to 15.7%) from 1994 onwards. The difference did not reach significance ($\chi^2 = 2.51$, P = 0.11). After 6 months of age, an estimated 5.0% (2.4% to 8.5%) of children who had not yet developed AIDS would do so each year.

Uptake of antiretroviral treatment increased significantly between 1995 and 1998, as did the proportion taking more than one antiretroviral drug (table 2). The proportion of mother-baby pairs receiving all three components of treatment¹ (antenatal, during delivery, and post partum to the baby) also increased significantly.

Table 3 shows that the risk of HIV transmission was significantly lower in infants with exposure to antiretroviral treatment than in those without. The effect of caesarean section was not significant after antiretroviral treatment was adjusted for. The baseline transmission rate among infants delivered vaginally or by emergency caesarean section in the absence of antiretroviral treatment was estimated to be 31.6%. Elective caesarean section or antiretroviral treatment alone reduced the transmission rate to 15.3% and 10.1%, respectively, and when combined reduced transmission to 4.2%.

Discussion

HIV vertical transmission rates rose gradually from 1984 to 1994 and then fell rapidly between 1995 and 1998. The earlier rise could be accounted for by changes in the epidemiology of HIV in infected women.⁵

Key messages

- Reliable estimates of HIV vertical transmission rates can be derived from surveillance data
- Infected pregnant women are increasingly taking up elective caesarean section and antiretroviral treatment to reduce the risk of transmitting HIV to their babies
- Vertical transmission rates have fallen greatly over the past four years and progression to AIDS among infected children may also have slowed
- These benefits can occur only if infected women are diagnosed before or during pregnancy

In the four years ending 1998, during which uptake of elective caesarean section and antiretroviral treatment was increasing, the estimated vertical transmission rate fell steeply to 2.2% (0% to 7.8%) in 1998. This is comparable with a 2.0% estimate based on a meta-analysis,² and 0.8% (1/133) in the French cohort⁴ among women taking antiretroviral treatment (mainly zidovudine only) and having an elective caesarean section. These findings are consistent with previously published data.¹⁰

Progression to AIDS (70% of which was *P carinii* pneumonia) within the first 6 months of life was reduced by nearly 60% in infants born after the beginning of 1994 compared with those born before. The effect was not significant, but a similar reduction of 66% in AIDS in infancy since 1993 was recently reported in the United States.¹¹ This change is likely to be due to prophylactic co-trimoxazole given to most children born to infected women from 6 weeks of age.^{7,8}

Prospective cohort studies tend to be set in specialist centres, whereas randomised trials may use exclusion criteria. National surveillance data have the advantage of being population based but are more likely to suffer from missing data and less frequent follow up. However, as long as bias caused by children of indeterminate status is removed, surveillance data should accurately reflect vertical transmission rates in clinical practice. Trials may, in any case, become increasingly difficult to carry out. Antiretroviral treatment is becoming increasingly diverse, more women will have received antiretroviral treatment before pregnancy, and the transmission rates now being reported are very low.¹²⁻¹⁵ If the possibility of teratogenic effects becomes a major concern,¹⁶ compliance with treatment regimens may fluctuate. Surveillance data may eventually become the most reliable way to monitor uptake of interventions and HIV vertical transmission rates.

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Contributors: TD elaborated the statistical methods, programmed them, carried out the analyses, and drafted the methods and results section. AEA obtained funding for the

surveillance (with Professor C S Peckham), conceptualised the analysis, and supported TD. TD and AEA are the guarantors. Introduction and discussion sections were drafted by DMG. PAT and JM assembled the surveillance data and assisted in its interpretation. All authors commented on all drafts of the paper.

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Endpiece

There when needed

God and the doctor we like adore
But only when in danger, not before;
The danger o'er, both are like requited,
God is forgotten, and the doctor slighted.

John Owen, c 1563-1622

Submitted by David Carvel, general practitioner
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