A retrospective case note review of the neonatal death of infants born to women living with HIV in the UK and Ireland 1998-2017

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Background

- Successful prevention strategies have driven the decline of the vertical transmission (VT) rate in the UK/Ireland from 2.1% in 2000-2001 to 0.28% in 2015-2016 [Figure 1].
- However, HIV-exposed uninfected children have been shown to be at increased risk of other adverse outcomes, particularly in the first few years of life.
- There is need for increased understanding into outcomes such as neonatal death (NND) in infants born to women living with HIV (WLWH).

Figure 1: Vertical transmission rates of HIV among diagnosed women 2000-16

Methods

- National Surveillance of HIV in Pregnancy and Childhood (NSHPC) is part of Public Health England’s Infectious Diseases in Pregnancy Screening Programme.
- All pregnancies to women living with HIV in the UK/Ireland are actively reported, along with their HIV-exposed infants and any children diagnosed with HIV (<16years).
- Neonatal death was defined as a live-born baby, who died before 28 completed days after birth
- Estimated yearly incidence of NND was reported for 1998-2017 and causes of NND coded using WHO ICD-PM classification.
- Risk factor analysis used multivariable logistic regression, including delivery year, maternal origin, maternal age, delivery CD4 count and viral load, antiretroviral therapy (ART) at conception, injecting drug use (IDU) and infant sex.
- A second analysis restricted to the years 2007-2017 was carried out, reflecting a time of improved reporting of delivery viral load.

Results

- Median maternal age at delivery was 31 years (IQR 27-35); other maternal characteristics are shown in Table 1.
- The overall NND rate was 4.1 per 1000 live-births (95% CI, 3.2-5.0), compared to an average of 3.24 in the general population (1998-2016).

Table 1: Maternal and pregnancy characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>Maternal region of origin</td>
<td></td>
</tr>
<tr>
<td>Africa</td>
<td>14146 (75)</td>
</tr>
<tr>
<td>UK/Ireland</td>
<td>2917 (15)</td>
</tr>
<tr>
<td>Other</td>
<td>1922 (10)</td>
</tr>
<tr>
<td>Timing of diagnosis</td>
<td></td>
</tr>
<tr>
<td>Before pregnancy</td>
<td>13469 (69)</td>
</tr>
<tr>
<td>During pregnancy</td>
<td>6132 (31)</td>
</tr>
<tr>
<td>ART at conception</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7836 (42)</td>
</tr>
<tr>
<td>No</td>
<td>10944 (58)</td>
</tr>
<tr>
<td>Viral load (copies/ml) at delivery</td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>8663 (76)</td>
</tr>
<tr>
<td>≥50</td>
<td>2689 (24)</td>
</tr>
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</table>

- 82 NNDs in total (18 [22%] without reported cause of death).
- 26 (32%) NNDs occurred within the first day of life (day 0).
- 104 individual causes of death were reported among remaining 64 NND cases [Figure 2].
- Prematurity was the leading cause of death, reported in 44% (28/64) cases, followed by congenital abnormality reported in 22 cases (34%).
- Most common abnormality was Trisomy 18 (6 cases)

Conclusions

- WLWH had a higher NND rate than the general population
- Detectable viral load and increasing calendar year were associated with increased risk and ART use at conception with decreased risk of NND
- Main cause of NND was preterm delivery

Risk factor analysis 1998-2017

- Only factor significantly associated with NND risk was ART at conception
  - Adjusted odds ratio (AOR) 0.57 (95% CI 0.30-0.99)

Restricted analysis (including delivery viral load 2007-2017)

- Delivery year (AOR 1.18 [95% CI 1.03-1.34] per 1 year increase) and detectable viral load (i.e. >50 copies/ml) (AOR 8.14 [95% CI 3.46-19.17] vs undetectable) were associated with increased NND risk
- Other AORs (all non statistically significant)
  - Maternal age ≥40 vs 24-39 years = 1.40 (95% CI 0.54-3.58)
  - Maternal IDU vs no IDU = 2.97 (95% CI 0.78-11.3)
  - CD4 <350 cells/mm³ vs ≥350 = 1.47 (95% CI 0.96-2.69)

- Limitations included lack of data on maternal substance use and weight, and lack of cause of death in 22% of cases
- Wide 95% CIs observed reflected small numbers of NNDs.
- Promotion of maternal viral load suppression through effective ART will not only improve maternal health and prevent VT, but may also reduce NND. The NSHPC continues to monitor NNDs.

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