Stillbirth in HIV-infected women delivering in UK/Ireland between 2007 and 2015

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Background and aims

- Stillbirth (SB) has multifactorial and incompletely understood causes. We previously reported that HIV-infected women delivering in the UK/Ireland had higher SB rates than the general population, at 1.1% between 1990-2006[1], a period spanning huge changes in characteristics and use of PMTCT interventions in this population[1-3].
- The aim of this work was to explore the current SB rate and associated risk factors in HIV-positive women delivering between 2007-2015 and reported to the NSHPC.

Methods

- Exclusion: Births at <24GW, multiple births.
- Definition: SB was defined as a baby delivered at ≥24 gestational weeks (GW) showing no signs of life.
- Period: 2007-2015 (reported to NSHPC up to Dec 2016).
- Multivariable Poisson regression with random effect to account for repeated pregnancies in the same mother to investigate whether maternal age, country of origin, year of delivery, IDU history, parity, first antenatal CD4 count ≤350cells/μL, antenatal ART regimen and late antenatal booking (≥13 GW) are risk factors associated with SB.

Results

- 10,316 singleton pregnancies were delivered at ≥24GW in 8069 mothers.
- 75.4% mothers were born in Sub-Saharan Africa.
- 49.4% pregnancies (4915) were conceived on ART.
- The most common antenatal ART regimens were PI/r- (5454, 55.0%) and NNRTI-based (2427, 24.5%); specific regimen was unknown in 4.6% pregnancies.
- ART regimen was switched in 1615 (16.3%) pregnancies.
- There were 43 (0.4%) cases of reported MTCT.
- 89 (0.9%) pregnancies ended in SB.
- There was no suggestion of a decline in SB reported to NSHPC over the time period (*P*=0.24).
- In contrast, the Office for National Statistics (ONS) for England and Wales reported a 0.5% SB rate for the same period.

		LB/ N(%) 10,316	SB/N(%) 89
Gender	Female	5126 (49.82)	28 (41.79)
	Male	5164 (50.18)	39 (58.21)
	missing	*26 (0.25)*	*22 (24.72)*
Gestational weeks	Median (IQR)	39 (38-40)	33 (27-37)
Birthweight (g)	Median (IQR)	3.10 (2.78-3.44)	1.98 (0.87-2.80)
SGA	No	7774 (77.88)	28 (45.16)
	Yes	2208 (21.12)	34 (54.84)
	missing	*334 (3.24)*	*27 (30.34)*
Congenital Abnormalities	No	9715 (97.15)	52 (85.25)
	Yes	285 (2.85)	9 (14.75)
	missing	*316 (3.06)*	*28 (31.46)*

Table 1 Characteristics of infants (singleton only) by live birth (LB) and stillbirth (SB)

Results

- SB infants were more likely to be male, pre-term, SGA and to have congenital abnormalities (Table 1)
- Multivariate analysis suggested significant risk factors for SB were antenatal CD4 count ≤350cells/μL and the mother being primiparous, older and originating from SSA or other world region (Table 2).

Table 2 Pregnancy characteristics by LB and SB and adjusted IRR for risk factors associated with SB

		LB/ N(%)	SB/ N(%)	IRR (95%CI)*
		10,316 (99.14)	**89 (0.86)**	
Delivery year	2007-2009	3843 (37.25)	41 (46.07)	1.00
	2010-2012	3591 (34.81)	30 (33.71)	1.15 (0.66, 2.01)
	2013-2015	2882 (27.94)	18 (20.22)	0.74 (0.36, 1.51)
Maternal age	<28 years	2237 (21.68)	12 (13.48)	1.00
	28-32 years	2471 (23.95)	23 (25.84)	3.38 (1.25, 9.16)
	33-36 years	2820 (27.34)	28 (31.46)	3.57 (1.31, 9.66)
	>36 years	2788 (27.03)	26 (29.21)	4.12 (1.49, 11.35)
Parity	Primiparous	2668 (27.18)	30 (37.50)	1.85 (1.10, 3.12)
	Multiparous	7147 (72.82)	50 (62.50)	1.00
Maternal origin	Europe/WEWC	1996 (19.57)	8 (9.30)	1.00
	SSA	7681 (75.32)	71 (85.56)	3.26 (1.07, 9.95)
	Other	521 (5.11)	7 (8.14)	5.59 (1.46, 21.48)
CD4 count	>350	6369 (65.74)	38 (48.10)	1.00
	≤350	3319 (34.26)	41 (51.90)	1.73 (1.05, 2.86)
ART at conception	No	4990 (50.56)	46 (56.10)	1.00
	Yes	4879 (49.44)	36 (43.90)	0.90 (0.51, 1.58)
Antenatal ART class	PI/r-	5406 (54.78)	48 (58.54)	1.00
	NNRTI-	2406 (24.38)	21 (25.61)	1.05 (0.57, 1.94)
	INSTI-	118 (1.20)	2 (2.44)	1.39 (0.19, 10.51)
	Other	335 (3.29)	0 (0.00)	-
	Switched	1604 (16.25)	11 (13.41)	0.74 (0.36, 1.55)

***N= 8984 – excludes multiple pregnancies and pregnancy with no ART described (483) and missing parity (457), origin (98) and CD4 (383). All IRR mutually adjusted (+for antenatal late booking and history of IDU) with random effect for mother.**

Conclusions

Despite continued declines in MTCT rates over this period (2007-2015) and increases in the proportion of HIV-positive women conceiving on ART and delivering with a suppressed viral load[3], the SB rate did not decline over these years and remains consistently higher in HIV-positive women than in the general population.

Geographical variability seen in SB rate across England and Wales in ONS data is mirrored in the HIV-positive population.

There are limitations to our study as the NSHPC does not routinely collect data on some important risk factors for SB, e.g. maternal BMI, socio-economic status, smoking and there were limited data to classify SB as antepartum or intrapartum. Also, details of SB tended to be underreported, as shown in Table 1.

To further understand the circumstances and risk factors for SB in HIV-positive women, the NSHPC plans to undertake an audit of pregnancies ending in SB (following established methodology used in an ongoing audit of cases in which MTCT occurred).

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NSHPC Ethics: MREC/04/2/009

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3. Peters et al, CID 2016

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