Pregnancies among women seen for HIV-clinical care - predictors and trends over time

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Background

- An increasing number of HIV-positive accessing HIV clinical care become pregnant [1,2]
- Diagnosed HIV-positive women accessing HIV clinical care in the UK include women of different ethnicities, ages and levels of morbidity
- The characteristics of this diverse group continue to change with an increasing number of older women and women on ART [3]

Research questions

1. Among women accessing HIV care, what factors are predictive of becoming pregnant?
2. Did the pregnancy incidence change during the period 2000-2009?
3. Are changes in the characteristics of pregnant women due to increases in the pregnancy rate among specific groups of women?

Methods

Data were obtained from two on-going studies:

- The UK Collaborative Cohort (UK CHIC) Study: a large cohort of adults accessing HIV clinical care at 13 HIV clinics, representing around 30% of women (aged 16-49 years) who accessed HIV care in the UK in 2000-2009 [4]
- The National Study of HIV in Pregnancy and Childhood (NSHPC): collates pregnancy data on HIV-positive women accessing antenatal care from all maternity units in the UK and Ireland using active surveillance [5]

Study design

- Women reported to both studies were identified using demographic and clinical variables including date of birth and CD4 counts
- A dataset was created containing all women (aged 16-49 years) who accessed care in 2000-2009 and included clinical data, such as CD4 counts (from UK CHIC), and antenatal data, such as date of delivery (from NSHPC)
- Age, ART use and CD4 count at start of year were used
- Pregnancies during which HIV was diagnosed were excluded from that year's data

Definitions

- *Date of conception:* estimated as 266 days before expected date of delivery
- *Year of pregnancy*: year of conception

Statistical analysis

- Predictors of pregnancy and changes in pregnancy incidence were assessed using generalized estimating equations (Poisson regression) and accounting for repeat measures
- Interaction terms between calendar year and each covariate were assessed to investigate whether calendar year trends varied in some subgroups

Results

- In 2000-2009 there were 1637 pregnancies among 1291 women
- The number of women accessing care increased each year, as did the number of pregnancies among this group (Table 1)

Changes in the characteristics of pregnant women

- During 2000-2009 there was an increase in the age of pregnant women, the proportion of black-African and black-Caribbean women and the proportion conceiving on ART
- There was a decrease in the proportion with CD4 <350 cells/mm^3 (p<0.001)

Predictors of pregnancy

- Older women were less likely to have a pregnancy than younger women (adjusted Relative Rate [aRR] 0.44 per 10 year increment in age [95% CI 0.41-0.46], p<0.001)
- Women with CD4<200 cells/mm^3 were less likely to have a pregnancy than women with CD4 200-350 cells/mm^3 (aRR 0.67 [0.56-0.79], p<0.001)
- Women of white or black-Caribbean ethnicity were less likely to have a pregnancy than women of black-African ethnicity (Table 2)
- ART use was not predictive of having a pregnancy after accounting for age, ethnicity and CD4 count (Table 2)

Changes in pregnancy incidence

- The likelihood that women had a pregnancy increased over the study period; this remained the case after accounting for changes in age, CD4 count, ethnicity and ART use (aRR per later year 1.05 [1.03-1.07], p<0.001)
- There was no evidence that the pregnancy rate increased more among women on ART, women of a particular age, ethnicity or CD4 category

Results

Table 1. Characteristics of pregnant HIV-positive women accessing care at UK CHIC sites

Year of conception		00/01	%	02/03	%	04/05	%	06/07	%	08/09	%
Women accessing care*		4555		6340		7901		9359		9942	
Pregnancy incidence		156	*3.4*	250	*3.9*	347	*4.4*	434	*4.6*	450	*4.5*
Repeat pregnancies		47	*30.1*	90	*36.0*	156	*45.0*	207	*47.7*	235	*52.2*
Age group (years)	16-25	16	*10.3*	45	*18.0*	56	*16.1*	68	*15.7*	69	*15.3*
	26-35	112	*71.8*	165	*66.0*	218	*62.8*	266	*61.3*	271	*60.2*
	36-49	28	*17.9*	40	*16.0*	73	*21.0*	100	*23.0*	110	*24.4*
On ART		72	*46.2*	127	*50.8*	179	*51.6*	225	*51.8*	287	*63.8*
CD4 count	≤200	31	*19.9*	35	14.0	*36*	*10.4*	44	*10.1*	37	*8.2*
	201-350	49	*31.4*	65	26.0	*98*	*28.2*	106	*24.4*	103	*22.9*
	>350	74	*47.4*	137	54.8	*204*	*58.8*	264	*60.8*	302	*67.1*
	NK	2	*1.3*	13	5.2	*9*	*2.6*	20	*4.6*	8	*1.8*
Ethnicity	Black-African	104	*66.7*	182	72.8	236	68.0	*322*	*74.2*	329	*73.1*
	Black-Caribbean	3	*1.9*	6	2.4	14	4.0	*18*	*4.1*	18	*4.0*
	White	35	*22.4*	30	12.0	48	13.8	*42*	*9.7*	48	*10.7*
	Other/NK	14	*9.0*	32	12.8	49	14.1	*52*	*12.0*	55	*12.2*

* Columns contain data for consecutive years, therefore women can be included twice in each column

Table 2. Predictors of pregnancy among women accessing HIV clinical care

Variables		Person years	Pregnancies	Rate /100 person yrs	95% CI	Adjusted Relative Rate*	95% CI	P-value
**Year of conception	00/01	4555	156	3.4	2.9 - 4.0	0.77	0.64-0.92	0.01
	02/03	6340	250	3.9	3.5 - 4.4	0.88	0.75-1.02	0.10
	04/05	7901	347	4.4	3.9 - 4.8	-	-	-
	06/07	9359	434	4.6	4.2 - 5.1	1.12	0.98-1.28	0.11
	08/09	9942	450	4.5	4.1 - 4.9	1.15	1.00-1.32	0.05
	All	38,097	1637	4.3	4.1 - 4.5	1.05	1.03-1.07	<0.001
Age group (years)	16-25	3486	254	7.3	6.4 - 8.1	1.12	0.98-1.29	0.11
	26-35	15,927	1032	6.5	6.1 - 6.9	1	-	-
	36-49	18,684	351	1.9	1.7 - 2.1	0.29	0.25-0.33	<0.001
On ART		22,512	890	4	3.7 - 4.2	0.95	0.85-1.05	0.32
CD4 count (cells /mm^3)	≤200	6073	183	3	2.6 - 3.4	0.65	0.55-0.77	<0.001
	201-350	8841	421	4.8	4.3 - 5.2	1	-	-
	>350	21,155	981	4.6	4.4 - 4.9	0.99	0.88-1.11	0.83
	NK	2028	52	2.6	1.9 - 3.3	0.52	0.39-0.68	<0.001
Ethnicity	White	6993	203	2.9	2.5 - 3.3	0.67	0.57-0.80	<0.001
	Black-Caribbean	1483	59	4	3.0 - 5.0	0.75	0.58-0.97	0.03
	Black-African	24,837	1173	4.7	4.5 - 5.0	1	-	-

* Including all variables listed in the table
** aRR relates to a 1 year increment

Study limitations

i. Some women in UK CHIC with a pregnancy may not have been found in NSHPC
ii. A higher proportion of women in UK CHIC accessed care in London than did nationally
iii. ART status did not take into account whether the woman was on ART for her own health or for prevention of mother-to-child-transmission (MTCT) during an earlier pregnancy

Conclusions

- HIV-positive women accessing HIV clinical care are increasingly likely to become pregnant.
- Changes in the characteristics of pregnant women in UK CHIC reflect changes in the characteristics of women accessing care
- Demand is likely to increase for the multidisciplinary services providing clinical and antenatal care, particularly services involved in the prevention and management of pregnancy complications, as an increasing number of older women have children - women at increased risk of pre-term delivery, pre-eclampsia and gestational diabetes, complications also associated with antenatal ART use
- MTCT rates in the UK are low, however the number infants exposed to HIV and ART *in utero* has increased. The long-term implications for *in utero* ART exposure, for children, and ART use during pregnancy, on the woman's health and future treatment responses are not completely understood and require further investigation

References:

1. Cliffe *et al*. *AIDS* Care 2011; **23**: 1093.
2. French *et al*. *JAIDS* 2012; **59**:287
3. HPA. SOPHID tables: 2010
4. www.ukchic.org.uk
5. www.nshpc.ucl.ac.uk

UK CHIC: ***Steering Committee:*** Jonathan Ainsworth, Jane Anderson, Abdel Babiker, David Chadwick, Valerie Delpech, David Dunn, Martin Fisher, Brian Gazzard, Richard Gilson, Mark Gompels, Phillip Hay, Teresa Hill, Margaret Johnson, Stephen Kegg, Clifford Leen, Mark Nelson, Chloe Orkin, Adrian Palfreeman, Andrew Phillips, Deenan Pillay, Frank Post, Caroline Sabin (PI), Memory Sachikonye, Achim Schwenk, John Walsh. ***Co-ordination****: UCL Research Department of Infection & Population Health, Royal Free Campus, London* (Teresa Hill, Susie Huntington, Sophie Josie, Andrew Phillips, Caroline Sabin, Alicia Thornton); *Medical Research Council Clinical Trials Unit (MRC CTU), London* (David Dunn, Adam Glabay). ***Participating Centres:*** *Barts and The London NHS Trust, London* (C Orkin, N Garrett, J Lynch, J Hand, C de Souza); *Brighton and Sussex University Hospitals NHS Trust* (M Fisher, N Perry, S Tilbury, D Churchill); *Chelsea and Westminster Hospital NHS Trust, London* (B Gazzard, M Nelson, M Waxman, D Asboe, S Mandalia); *Health Protection Agency – Centre for Infections London (HPA)* (V Delpech); *Homerton University Hospital NHS Trust, London* (J Anderson, S Munshi); *King's College Hospital NHS Foundation Trust, London* (H Korat, J Welch, M Poulton, C MacDonald, Z Gleisner, L Campbell); *Mortimer Market Centre, London* (R Gilson, N Brima, I Williams); *North Middlesex University Hospital NHS Trust, London* (A Schwenk, J Ainsworth, C Wood, S Miller); *Royal Free NHS Trust and UCL Medical School, London* (M Johnson, M Youle, F Lampe, C Smith, H Grabowska, C Chaloner, D Puradiredja); *St. Mary's Hospital, London* (J Walsh, J Weber, F Ramzan, N Mackie, A Winston); *The Lothian University Hospitals NHS Trust, Edinburgh* (C Leen, A Wilson); *North Bristol NHS Trust* (M Gompels, S Allan); *University of Leicester NHS Trust* (A Palfreeman, A Moore); *South Tees Hospitals NHS Foundation Trust* (D Chadwick, K Wakeman). **NSHPC: Co-ordination:** Pat Tookey, Janet Masters, Claire Townsend, Hiwot Haile-Selassie, Icina Shakes & Claire French. We gratefully acknowledge the contribution of the midwives, obstetricians, genitourinary physicians, paediatricians, clinical nurse specialists and all other colleagues who report to the NSHPC through the British Paediatric Surveillance Unit of the Royal College of Paediatrics and Child Health, and the obstetric reporting scheme run under the auspices of the Royal College of Obstetricians and Gynaecologists. Ethics approval for NSHPC was renewed following review by the London Multi-Centre Research Ethics Committee in 2004 (MREC/04/2/009). **Sources of Funding:** UK CHIC is funded by the Medical Research Council (MRC), UK (grants G00001999 and G0600337). NSHPC receives core funding from the Health Protection Agency (grant number GHP/003/013/003). Data is collated at the UCL ICH which receives a proportion of funding from the Department of Health's National Institute for Health Research Biomedical Research Centres funding scheme. Susie Huntington has a UCL Studentship, funded by the MRC, for postgraduate work. Claire Thorne holds a Wellcome Trust Research Career Development Fellowship.