

The prevalence of human retroviral infections in female patients attending a central London sexually transmitted disease clinic: 1985-1990

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Abstract

Objectives—To determine the prevalence of infection with HIV-1, HIV-2, HTLV-1 and HTLV-2 in female attenders at a central London sexually transmitted disease clinic in an 8 week period in 1989-1990, and compare it with similar samples studied between 1985 and 1987.

Design—Anonymous testing of serum samples from consecutive female patients having routine serological investigation for syphilis. Testing was for clinically important retroviruses, Hepatitis B core antibodies (anti-HBc), and p24 and reverse transcriptase (RT) antigens. Age (in 5 year bands), nationality (in broad geographical zones), diagnosis on the day of presentation, and history of intravenous drug usage were recorded for each patient. Annual gonorrhoea rates were analysed from 1981 to 1990.

Setting—Outpatients of the department of genitourinary medicine.

Patients—A total of 850 females attending consecutively and having routine syphilis serology.

Main Results—The prevalence of anti-HIV-1 in female attenders in 1989-1990 was 0.35% (3/850). Prevalence in the same clinic has remained statistically unchanged since the first female cases were identified in 1986. No cases of HIV-2, HTLV-1 or HTLV-2 were identified, and no early HIV-1 infection evidenced by the presence of p24 or RT antigenaemia was found. Female gonorrhoea rates continued to decline but other STD monthly/annual rates have remained unchanged.

Conclusions—Over the last 5 years prevalence of HIV-1 infection in females in our clinic has remained unchanged and other retroviral infections have remained absent. However, the unaltered rates of other genital infections, their potential role in the heterosexual spread of HIV-1 infection, and the lack of evidence for any major changes in female sexual behaviour suggests there is a need to remain vigilant. This work complements the MRC multi-centre, unlinked, genitourinary medicine clinic, anonymous testing programme, and our group will continue to apply this simple methodology to specimens from female attenders to contribute to the surveillance of the evolving HIV-1 epidemic.

Introduction

Worldwide, the commonest mode of transmission of HIV-1 and HIV-2 is by heterosexual intercourse,¹ initially reported for Sub-Saharan Africa² and more recently in South America,³ the USA⁴ the UK⁵ and South East Asia.⁶ Prostitution, frequency of partner change,⁷ genital mucus membrane damage,⁸ STD frequency,⁹ and altered host resistance^{10 11} have all been implicated as important factors associated with high rates of spread. Data from the USA, where the epidemic is 4 years further advanced than the UK, suggest a relentless rise in AIDS and HIV-1 infection in the heterosexual population; at present female AIDS cases associated with heterosexual exposure are 3.42% (6460/188,348) of the total.¹² Represented in this group of cases are those with risk factors associated with birth or sexual contact in a pattern II country,¹² those with no risk factors, and those due to spread of infection by sexual partners belonging to primary risk groups.¹³ Certainly the present numbers indicate that the new cases of AIDS in heterosexuals will continue to rise well into the next century.¹⁴

Studies in the UK carried out amongst STD clinic patients,¹⁵⁻¹⁷ antenatal clinic attenders^{18 19} and babies²⁰⁻²² have already revealed a small but consistent presence of HIV-1 infection in the heterosexual population. Many of these studies used anonymous testing, a method regarded as important where there is a low prevalence, to avoid compliance bias and ensure accurate surveillance data.^{23 24}

The aims of this anonymous study were firstly, to examine the trends in the prevalence of HIV-1, HIV-2, HTLV-1 and HTLV-2 in female STD clinic attenders and, secondly, to establish a baseline for further application of this simple methodology for future surveillance of the heterosexual HIV epidemic in this population.

Methods

During an 8 week period between November 1989 and January 1990 we studied 850 consecutive female patients attending the department of genitourinary medicine at The Middlesex Hospital, London and having routine serological tests for syphilis. Patients already attending the clinic as part of routine follow-up of HIV-1 infection were excluded. Age (in 5 year bands), nationality (in broad geographical zones: UK, rest of Europe, North America, Central/South America, Australasia, North Africa, Sub-Saharan Africa, India, Far

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Accepted for publication 13 August 1992

Table 1 Demographic features of females seen during 1987 and 1989–1990 study periods

	1987	1989–1990
No of females seen	412	850
No (%) not born in UK	94 (22.8)	210 (24.7)
No (%) anti-HIV-1 positive	4 (0.97)	3 (0.35)
Mean age (range) years	25 (17–67)	26.8 (15–70)*
No (%) total anti-HBc positive	40 (9.7)	36 (4.0)
No (%) UK anti-HBc positive	19 (4.6)	24 (3.7)

No = number

*calculated from mid-point of 5 year age bands

[Similar data not collected in 1985 and 1986]

East, Mediterranean and others), diagnosis on the day of presentation and history of intravenous drug usage were taken from computer files and recorded on numbered record sheets. Anonymity was ensured by removing the patients clinic number from the record sheets and substituting a serum code number before results were analysed. This methodology was different from previous samples: in 1985 and 1986 no data were collected, and in 1987 when data were collected directly from notes. These changes were established to preserve anonymity but retain some basic information of value in future data analysis.

Serum samples were tested for anti-HIV-1 by a competitive enzyme-linked immunosorbent assay (ELISA: Wellcozyme HIV-1, Wellcome Diagnostics), for anti-HIV-2 by an immunometric HIV-1+2 ELISA (Wellcozyme HIV-1+2, Wellcome Diagnostics), for anti-HTLV-1 and 2 by gelatin particle agglutination (Serodia, Fujirebio, Inc) and for anti-HTLV-1 by an in-house competitive ELISA. All potential retrovirus antibody positive sera were confirmed by Western Blot analysis (Dupont Ltd). Only anti-HIV-1 positive sera from previous samples in 1986 and 1987 were available for testing for HTLV-1 and 2.

HIV-1 p24 and reverse transcriptase (RT) antigens, markers of infection present prior to seroconversion, were measured using in-house ELISAs^{25 26} by initially testing pools of 12 sera and further investigating those pools showing signal above test cut-off.

Hepatitis B core antibodies (anti-HBc) were measured by a modified passive haemagglutination assay (Green Cross Corporation) and confirmed by an in-house radioimmunoassay.

The annual gonorrhoea rate (number of females with gonorrhoea over the total number of female cases reported on the KC60 Depart-

ment of Health quarterly returns) were analysed for women from 1981 to 1990.

Ethical committee approval was obtained in 1985 and 1987 as part of ongoing anonymous point prevalence studies to examine the changing prevalence of retroviral infections in our clinic attenders. Data were analysed by Mann-Whitney U test for differences in continuous variables and chi squared test for differences in proportions.

Results

In 1989–90 three of 850 women studied were anti-HIV-1 seropositive, an overall prevalence of 0.35% (table 1). This figure remains statistically unchanged since the first female cases were identified in our clinic population (0.5% in 1986; 0.97% in 1987; table 2). The three patients found in the present study were significantly older than the sample population (analysis was based upon the mid point figure for each positive case: $p=0.021$); all were anti-HBc negative, and one had gonorrhoea at the time of testing. There was no significant difference in age, proportion of UK nationals and percentage of other nationalities in this sample and previous samples studied.

No patients in the 1989–1990 sample or previously identified anti-HIV-1 antibody positive females were seropositive for HIV-2, HTLV-1 or HTLV-2. Further, no markers of early HIV-1 infection (p24 and RT antigens) were detected in any samples.

The gonorrhoea rate (fig 1) had fallen from 3.84% (310/8054) in 1981 to 0.71% (66/9189) by the end of 1989 ($p < 0.01$), a decline of 0.35% per year. It then rose to 0.89% (79/8813) in 1990 (not significant).

The prevalence of anti-HBc in all females attending was 4.0% (36/850) and 3.7% (24/640) in UK attenders. These figures were significantly lower than previous samples: 1987 total—9.7%, UK—4.6% ($p < 0.001$); 1986 total—9.1%, UK—4.7% ($p < 0.001$).

Of 850 females in the 1989–1990 sample 515 (61.0%) had a genital infection requiring inclusion in the annual clinic returns on the day of testing (table 3) and 240 (28.0%) of the total sample had conditions likely to produce some loss of integrity or inflammation of the genital tract mucus membranes (table 3: numbers 2–7) compared with the 1987 sample when 271/412 females (65.5%) had a genital infection and 106 (25.7%) fell into the latter

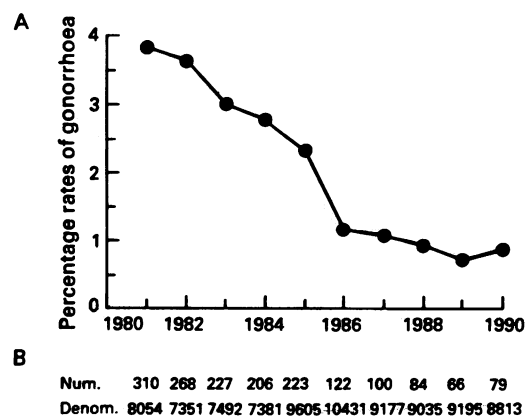
Table 2 Seroprevalence and demographic features for anti-HIV1 seropositive females between 1985–1990

Year	Seroprevalence	Age or range (years)	Nationality	Diagnosis on the day	Anti-HBc	HIV risk
1985	0/133	—	—	—	—	—
1986	2/395	28	UK	NK	NEG	NONE
		23	UK	NK	POS	IVDU
1987	4/412	23	UK(SSA)	NSU contact	NEG	NONE
		33	UK(Europe)	HIV test	NEG	NONE
		22	UK	WARTS	NEG	NONE
		26	UK	NAD	POS	IVDU*
1989–1990	3/850	36–40	UK	NK	NEG	NONE
		31–35	SSA	GC	NEG	NONE
		41–45	UK	NAD	NEG	NONE

UK = United Kingdom resident; NK = not known; NEG = negative; POS = positive; GC = gonorrhoea; UK() = birth place IVDU = intravenous drug user; NAD = no abnormality detected; SSA = Sub-Saharan Africa

* last use of drugs >3years ago.

Figure Percentage (a) and numerical fractions (b) for rates of gonorrhoea for female (●) attenders at the Middlesex Hospital, London during 1981–1990. Num. = numerator, Denom. = denominator.



category (no significant differences).

Overall, there were no differences in the monthly rates of genital infections (monthly case number/total monthly cases) between the 1987 and 1989–1990 samples. During the course of the present study 84 (9.9%) of females attenders requested an HIV-1 antibody test; similar figures were not available on earlier samples.

Discussion

The anti-HIV-1 seroprevalence (0.35%) in this sample was statistically unchanged since 1986 when the first positive females were identified at our clinic.¹⁵ These positive cases were older than in previous years which may be relevant in terms of epidemic evolution. There was no evidence of HIV-2, HTLV-1 or HTLV-2 infection in the present or previous samples, and the absence of p24 and RT antigens excluded the possibility of pre-seroconversion cases in this study sample. This seroprevalence for heterosexual females in STD clinic attenders in London is in agreement with other recent studies.^{17 27}

Surrogate markers to detect possible changes in sexual behaviour revealed apparently contradictory results in this study. The gonorrhoea rates continued to fall significantly up to 1989, and then rose in 1990, a change that was not significant but may reflect observations by

Table 3 A comparison of the proportions and monthly rates of genital infections (GI)* during the study periods amongst 412 females in 1987 (1 month) and 850 females 1989–1990 (2 months)

	1987 (number/%)	1989–1990 (numbers/%)
Total with GI diagnosis	271/65.3%	515/61%
Total with no GI diagnosis	141/34.7%	335/39%
1. Total with vaginal candida	37/9%	155/18%
2. Total with chlamydia	35/8.5%	95/11%
3. Total with genital warts	37/9%	66/8%
4. Total with genital herpes†	22/5%	38/4.5%
5. Total with trichomoniasis	8/2%	29/4%
6. Total with gonorrhoea	1/0.2%	10/1%
7. Total with syphilis	3/0.7%	2/0.2%
8. Total unspecified	128/31%‡	36/4%
9. Total requesting an HIV test	not recorded	84/10%

* data represents the principal diagnosis on day of presentation

†primary and recurrent attacks

‡data will include those requesting an HIV test

§Monthly rate: in 1987 number equals the monthly rate; in 1989–1990 number/2 equals the monthly rate.

others that show a reversal in the declining gonorrhoea rates seen in the last 5 years.²⁸ The prevalence of anti-HBc was statistically lower in the 1989–1990 sample (4.0%) compared with previous samples (1987—9.7%; 1986—9.1%) but no changes were observed in the monthly rates of other STDs during the study periods. The fall in anti-HBc prevalence cannot entirely be accounted for by changes in the proportion of UK to non-UK females in the sample²⁹ and we find it difficult to believe that such a fall within 2 years in a persistent marker of Hepatitis B virus infection was a reflection of changing sexual behaviour; this observation is being further investigated. The unchanged monthly, and annual rates (not presented here) of genital infections, especially those associated with some degree of damage to genital tract mucus membranes give cause for concern. The ulcerating STD associated with *Haemophilus ducreii* has been suggested as a co-factor in HIV-1 transmission in Africa and the USA,^{30 31} and other pathogens like herpes simplex virus³² and *Treponema pallidum*³³ have been similarly implicated. Further, in a prospective study in African prostitutes⁹ seroconversion for anti-HIV-1 in individuals with low incidence of ulcerating STDs was significantly associated with non-ulcerating STD pathogens (*Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*) during the period preceding seroconversion, and the authors suggest a causal association. The mechanism in both these situations is, at least in part, presumed to be disruption in the integrity of normal skin or mucosa. The role of all these pathogens in HIV-1 transmission is made more important by the recent work of Haseltine *et al*^{34 35} demonstrating that tissue dendritic cells which are phagocytic, CD4 positive, antigen-processing cells of the reticuloendothelial system in the genitourinary (GU) and gastrointestinal (GI) tracts become infected with HIV-1 and produce 50 times as much virus as infected CD4 positive lymphocytes. They proposed that these cells may be infected locally in GU and GI tracts by HIV-1 and then present intact virions to other cells of the immune system (that is, helper lymphocytes and macrophages) at sites distant from the site of infection.³⁴ Thus, any pathogen inducing a local inflammatory reaction in these sites, where tissue dendritic cells are part of the inflammatory infiltrate may serve as a co-factor for co-existing HIV-1 to infect the host. This evidence, together with data from elsewhere that heterosexual populations continue to engage in high risk sexual activities^{36 37} and show a significant but relatively poor increase in condom usage^{38 39} have led us to conclude that those carrying out population serosurveillance must remain vigilant.

The implication of an evolving heterosexual epidemic with a viral agent that is transmitted by sexual intercourse,¹ has a significant rate of vertical transmission,⁴⁰ is presently incurable, and ultimately fatal, is that it is not only a threat to individuals but eventually whole populations. Our group has been one of the pioneers in developing laboratory methods and

strategies for serosurveillance of HIV-1 infection in the UK since 1982;^{15 16 20-22 25 41-44} much of this work has now devolved to others, for example the MRC multicentre, unlinked, genitourinary medicine clinic, anonymous testing programme.^{24 45} Using our present methodology, which is complementary to such studies by providing additional local data on the prevalence of human retroviral infections in our sexually active female population, we will continue to contribute to the overall serosurveillance of the evolving epidemic.

The authors thank all staff in the Division of Virology and Department of Genitourinary Medicine, past and present, who have contributed, and without whom this work would not be possible.

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