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INFECTIOUS DISEASES

Differences between women and men in serial HIV prevalence and incidence trends

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Abstract To measure trends in HIV incidence and serial prevalence by sex in a intravenous drug users (IDUs) and heterosexuals (HT) cohort recruited in a counselling centre in Valencia (1988–2005). Serial prevalence and incidence rates were calculated and modelled by logistic and Poisson regression respectively. 5948 IDUs and 13343 HT were recruited. Prevalence was higher among female IDUs (46% vs. 41%), and female HT (4.1% vs. 2%). For IDUs, an interaction ($P = 0.005$) between sex and calendar was detected. Age-adjusted prevalence showed faster yearly decline in men (OR = 0.87 95%CI: 0.85–0.88) than in women (OR = 0.91 95%CI: 0.88–0.93). Incidence was higher in female IDUs (9.79% p-y) than in men, (5.38% p-y) with an annual decrease for both of 11%. HIV incidence was higher in female HT (0.62% p-y) compared to men 0.23% p-y with a 21% yearly decline. Gender differences in HIV prevalence and incidence trends have been detected. Women showed an increased vulnerability to infection in a country whose HIV epidemic has been largely driven by IDUs.

Keywords HIV testing · HIV incidence and prevalence · Trends · Gender

Abbreviations

CIPS	Centre for AIDS Information and Prevention
HT	Heterosexuals
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCV	Hepatitis C virus
IDU	Intravenous drug users
RR	Rates ratio

Introduction

The proportion of women living with HIV has gradually increased over the last decade in most parts of the world [1]. Women are known to be more vulnerable to becoming HIV infected, both biologically and socially, and gender disparities have been pointed out as the main determinants for the disproportionate increase of new HIV infections in women [2].

Of the approximate 20,000 new HIV diagnoses in Western Europe in countries with available data by 2004, 35% were women and 91% of them had become infected through unprotected heterosexual contacts [3]. In USA, the number of HIV infected women is estimated to have increased by 15% from 1999 to 2003 compared to 1% in

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the men during the same period [4]. UNAIDS warns that, for many women, the main risk factor for HIV infection is related to their male partners' sexual behaviours [5].

The Spanish HIV epidemic has been characterized by extremely high rates in injecting drug users (IDUs) from the mid 80s to current date [6, 7]. The proportion of women among AIDS cases has been around 20% and, in the last years, the proportion of sexually transmitted cases has increased drastically at the expense of a decrease of AIDS cases in IDU [8]. As for HIV infections, the proportion of women among HIV diagnoses in the Spanish regional HIV registries is around 25–30%. Castilla et al. have estimated that HIV incidence rates by 2004 in the general Spanish population were of 32 cases per million in women and 84 cases per million in men [9].

In a recently published article looking at trends in HIV incidence and prevalence in people attending a Centre for Information and AIDS Prevention (CIPS) in Valencia we report important decreases in HIV transmission in all transmission categories, particularly in IDUs, but did not explore differences by sex [10]. The objective of this study is to measure the magnitude and the trends in HIV incidence and serial prevalence by sex in a large cohort of IDUs and heterosexuals (HT) who underwent voluntary testing for HIV infection in a CIPS from 1988 to 2005.

Subjects and methods

Open cohort study of all subjects who underwent voluntary HIV testing and counselling in the CIPS of Valencia, the third largest city in Spain, from 1988 to 2005. For the purpose of these analyses, only IDUs and HT were included. This centre provides HIV information and counselling, free and anonymous HIV testing, as well as testing for Hepatitis B virus (HBV), Hepatitis C virus (HCV), Hepatitis A virus (HAV) and syphilis. A soundex code which include date of birth, sex and name and surname initials was used to identify individuals uniquely and to link subject tests. Previous to HIV testing, a personal face-to-face interview is carried out by health professionals where information on different socio-demographic variables as well as on risk practices is collected. They also receive information and counselling on preventive measures, both pre-test and post-test. Subjects are also offered vaccination against HAV and HBV. Subjects who report high risk practices are invited to attend the centre every 6 months. Further information on the study has been previously described in more detail [10]. HIV antibodies were determined through enzimoinmunoanalysis and confirmed by Western Blot. Risk category-transmission has been grouped in three mutually exclusive categories: intravenous drugs users (IDU), men who have sex with men (MSM) and HT. A separated analysis for UDI and HT categories has been carried out.

Statistical analyses

We have considered as prevalent subjects testing HIV positive on first visit to the CIPS. These data have been used to calculate serial HIV prevalence (the percentage of HIV+) for each year for men and women separately. We have considered as incident HIV negative subjects testing HIV positive in a subsequent visit within 3 years from the HIV negative result. We have assumed that the seroconversion date is the mid-point between the last negative visit and the first positive visit. The annual rates of HIV incidence have been calculated, accounting for identified seroconverters in the numerator, and the persons- time at risk for seroconversion as denominator (follow up time for those who had further visits to the CIPS and maintained HIV negative in successive visits, and time from first HIV-negative visit to estimated seroconversion date for those identified as seroconverters). Calendar time has been divided into periods according to antiretroviral availability.

1988–1990 (no treatment or monotherapy), 1991–1996 (monotherapy or combination therapy), 1997–2000 (early HAART era), and 2001–2005 (HAART era).

The evolution of both the serial prevalence and incidence of HIV by sex and calendar periods in IDUs and HT was explored. After plotting serial HIV prevalence by calendar time, we fitted a Jointpoint regression model to identify points with a significant change in the trend [11]. A model in logarithmic scale was used (log prevalence $= \beta \times$ time). The analysis started by allowing a minimum number of changes (none, for example) and contrasting the existence of one or more changes (up to 3). Once change points are identified, logistic models are then fitted. Results are expressed in odds ratio (OR) with 95% confidence interval.

Poisson regression was used to estimate HIV incidence adjusting by age, sex, transmission category and calendar time. Results are expressed in rates ratio (RR) with 95% confidence interval. A Jointpoint regression model, software from Surveillance Research Program of US National Cancer Institute was fitted to identify significant points of change [12].

Interactions between sex and the other exposure variables (age, transmission category and calendar period) have been looked for. The results of the best models are shown graphically for men and women from different transmission categories. Year 1990 was considered the baseline as we anticipated that during 1988–1990 all previously untested HIV prevalent cases may have contributed to biased estimates of the prevalence estimates in that first period.

For calculating prevalences and incidences regression models, we used the STATA 8.0 programme [13]. Statistical significance was established at $P = 0.05$ comparing the maximum likelihood values.

Results

Of the 5,948 IDUs who attended the CIPS, 22% were women, and of the 13,343 HT, the proportion of females was 46%. The women in this study, both IDUs and HT, were younger than the men on their first visit to the CIPS (Table 1). A decrease in the number of IDUs attending this centre from 1980 to 2005 is observed for both male and female IDUs as results of an increase in the number of HT (Table 1).

Among IDUs, HIV prevalence for the whole study period was significantly ($P = 0.005$) higher in the women, 46%, compared to the men, 41%. For both sexes, HIV serial prevalence was highest among aged 26–35 years. HIV serial prevalence was considerably lower in HT than in IDUs. Also in HT, HIV prevalence was higher in women, 4.1%, than in men, 2% (Table 2).

Table 1 Descriptive characteristics of the women and men who underwent voluntary HIV testing in the Information and Prevention Centre (CIPS) of Valencia (1988–2005)

Transmission category	Female	Male	Overall
IDUs[a]	1336 (22.5%)	4612 (77.5%)	5948
Age group*			
15–25 years	599 (44.8%)	1648 (35.7%)	1835 (30.9%)
26–35 years	625 (46.8%)	2461 (53.4%)	3339 (56.1%)
More 36 years	112 (8.4%)	503 (10.9%)	774 (13.0%)
Calendar year*			
1988–1990	434 (32.5%)	1247 (27.1%)	1681 (28.3%)
1991–1996	619 (46.3%)	2202 (47.7%)	2821 (47.4%)
1997–2000	196 (14.7%)	813 (17.6%)	1009 (17%)
2001–2005	87 (6.5%)	350 (7.6%)	437 (7.3%)
HTs[b]	6100 (45.7%)	7243 (54.3%)	13343
Age group*			
15–25 years	2766 (45.3%)	2493 (34.4%)	5259 (39.4%)
26–35 years	2397 (39.3%)	3151 (43.5%)	5548 (41.6%)
More 36 years	938 (15.4%)	1598 (22.1%)	2536 (19.0%)
Calendar year*			
1988–1990	318 (5.2%)	247 (3.4%)	565 (4.2%)
1991–1996	1956 (32%)	2308 (31.9%)	4264 (32%)
1997–2000	1455 (23.9%)	1967 (27.2%)	3423 (25.7%)
2001–2005	2371 (38.9%)	2720 (37.5%)	5091 (38.2%)

[a] Injected drugs users

[b] Heterosexual

*P-value < 0.001

Figure 1a displays the evolution overtime of HIV serial prevalence for both male and female IDUs. Although both groups start off from high HIV prevalence values, ~55%, and both show a marked decrease over time, this decline is less marked in the women. No changes in this decreasing trend are detected after fitting a Jointpoint regression model. In the multivariate logistic regression model looking for determinants of HIV serial prevalence, a statistically significant interaction ($P = 0.005$) between sex and calendar year was detected in IDUs. As previously observed in crude analyses from Table 1a, the age-adjusted HIV serial prevalence also showed a faster yearly decline in men (OR = 0.87 95%CI: 0.85–0.88) than in women (OR = 0.91 95%CI: 0.88–0.93) (Table 3).

Figure 1b displays the evolution of HIV serial prevalence over time for both male and female HT. For both groups, HIV prevalence is higher in initial years and decreases overtime with no significant changes in the trend detected after fitting a Jointpoint regression model. Women show a clearly higher HIV prevalence throughout the whole period which is 119% (OR = 2.19 95%CI: 1.77–2.71) higher than the men's. A 11% yearly decrease for both sexes in HIV prevalence is observed in the multivariate logistic regression model (Table 3).

Among IDUs, 265 HIV incident cases were detected over 5140.5 persons-year (p-y) time of observation. HIV incidence for the whole period was higher in women, 7.66 per 100 p-y than in men, 4.52 per 100 p-y (RR = 1.28 95%CI: 0.98–1.67) (Tables 2 and 4). A decreasing trend in HIV incidence was observed for men and women (Fig. 2a); with an annual decrease of 11% (RR = 0.89 95%CI: 0.86–0.92) in multivariate Poisson regression (Table 4).

A lower HIV incidence was observed among HT, 32 cases during 7630.9 persons-year time of observation. Although HIV incidence was higher in women, 0.62 per 100 p-y compared to men 0.23 per 100 p-y, differences were not statistically significant, RR 1.56 (95%CI: 0.71–3.42) (Table 4). For both men and women, a 21% yearly decline in HIV incidence is observed overtime, with no changes in this trend detected by Jointpoint regression (Fig. 2b).

Discussion

We have detected gender differences in the magnitude and in the trends of HIV serial prevalence and HIV incidence in both IDUs and HT who access voluntary testing in an AIDS prevention and information centre. Women, irrespective of their transmission mechanisms, had higher HIV prevalence and incidence than men. For all groups, important declines in HIV serial prevalence and HIV incidence were observed from the late 90s to 2004 but trends were different for men and women.

Table 2 Prevalence and incidence of HIV infection by transmission category in the women and men who underwent voluntary HIV testing in the Information and Prevention Centre (CIPS) of Valencia (1988–2005)

	Prevalence (95%CI)				Incidence (95%CI)			
	N	Female	*N*	Male	*N*	Female	*N*	Male
IDUs[a]								
Age group								
15–25 years	233	38.9 (34.9–42.8)	530	32.2 (29.9–34.4)	56	9.79 (7.53–1.27)	108	5.38 (4.45–0.6.49)
26–35 years	332	53.1 (49.2–57.0)	1122	45.59 (43.6–47.6)	21	5.4 (3.57–0.8.41)	73	3.91 (3.11–0.4.91)
More 36 years	45	40.2 (31.1–49.3)	227	44.7 (40.3–49.0)	2	2.63 (0.65–10.5)	5	2.15 (0.89–5.18)
Calendar year								
1988–1990	226	52.1 (47.4–56.8)	671	53.8 (51.0–0.56.9)	14	10.8 (6.42–18.3)	36	10.4 (7.56–14.5)
1991–1996	292	47.2 (43.2–51.1)	900	40.9 (38.8–42.9)	44	8.65 (6.44–11.6)	93	4.6 (3.83–5.75)
1997–2000	65	33.2 (26.6–39.7)	231	28.4 (25.3–31.5)	16	5.86 (3.58–9.56)	39	3.19 (2.33–4.36)
2001–2005	27	31 (21.3–40.7)	77	22 (17.6–26.3)	5	4.15 (1.73–9.99)	18	3.18 (2.01–5.06)
HTs[b]								
Age group								
15–25 years	86	3.11 (2.46–3.76)	30	1.20 (0.78–1.63)	13	0.71 (0.41–1.22)	2	0.12 (0.03–0.51)
26–35 years	124	5.18 (4.29–6.06)	69	2.19 (1.68–2.70)	9	0.63 (0.32–1.21)	4	0.25 (0.09–0.66)
More 36 years	42	4.47 (3.15–5.79)	44	2.75 (1.95–3.56)	1	0.23 (0.03–0.1.64)	3	0.38 (0.12–1.18)
Calendar year								
1988–1990	24	7.55 (4.64–10.4)	17	6.88 (3.73–10.04)	3	2.20 (0.71–6.85)	0	0
1991–1996	124	6.34 (5.26–7.42)	62	2.69 (2.03–3.35)	15	1.21 (0.73–2.01)	5	0.43 (0.18–1.04)
1997–2000	51	3.51 (2.56–4.45)	31	1.58 (1.03–2.13)	3	0.28 (0.09–0.87)	3	0.22 (0.07–0.68)
2001–2005	53	2.24 (1.64–2.83)	33	1.21 (0.80–1.62)	2	0.16 (0.04–0.63)	1	0.07 (0.01–0.52)

[a] Injected drugs users

[b] Heterosexual

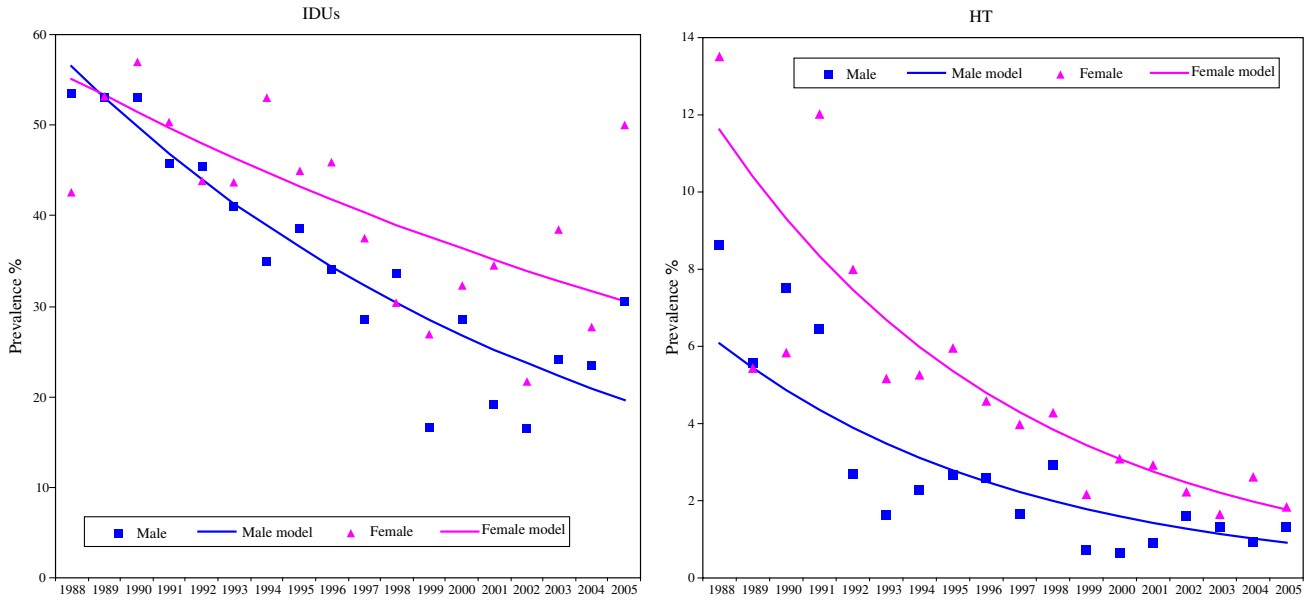

Fig. 1 HIV serial prevalence trends by sex in IDUs and HTs attending the CIPS for their first time between 1988 and 2005. Joinpoint regression fitted

As expected, IDUs had a much higher prevalence of HIV infection than HT. The magnitude of the HIV prevalence we have detected for both transmission categories is very high, but coincides with the work published earlier in similar settings in Spain. Female IDUs had higher HIV prevalence and showed a slower decline in HIV serial

Table 3 Prevalence odds ratio of HIV infection by calendar year and sex after fitting a logistic regression model

	OR[a] (95%CI)	
	IDUs	HTs
Calendar year	0.866 (0.852–881)	0.89 (871–910)
Sex		
Male	1	1
Female	1.11 (0.94–1.30)	2.19 (1.77–2.71)
Interaction between calendar year and gender	1.04 (1.01–1.08)	

[a] Adjusted for age

Table 4 Relative incidence rate of HIV infection by calendar year and sex after fitting a Poisson regression model

	RR[a] (95%CI)	
	IDUs	HTs
Calendar year	0.89 (86–0.92)	0.79 (0.73–0.87)
Sex		
Male	1	1
Female	1.28 (0.98–1.67)	1.56 (0.71–3.43)

[a] Adjusted for age

prevalence than men. The female IDUs in our study also had a higher HIV incidence than male IDUs though trends overtime, though descending, did not differ by sex. The higher HIV incidence, and thus prevalence, in female IDUs has been described in other settings [10, 14] as may be explained by women's increased vulnerability to sexual transmission of HIV. Also, female IDUs have additional HIV sexual exposures, as commonly, their partners are HIV-infected male IDU and they are frequently forced to engage in sex work to pay for both her and her partner's drug use [15, 16]. For HIV prevalence in HT, women also elicited higher values all along the period but the decline of HIV serial prevalence overtime was faster than men's, as was their HIV incidence.

HIV incidence was higher in female IDUs than in males showing extremely elevated rates in the late 80s, 14 cases per 100 p-y and 9 cases per 100 p-y for women and men respectively. For both, a significant decline is seen, though incidence remains unacceptably high, with four and two new HIV infections per 100 p-y respectively. For HT, women started off at very high incidence rates, 3.5 per 100 p-y by 1989, and show a steep decline in the mid-nineties and remain below 0.5 cases per 100 p-y. These incidence rates are, nevertheless, very high but the pattern resembles that of a cohort study of IDU, from Baltimore in which HIV incidence was estimated to be 4.57 per 100 p-y in 1988 and 0.53 per 100 p-y in 2004 [17].

To better understand our findings, the profile and evolution of the people attending this centre for voluntary testing merits further thought as the selection processes operating in the population explain some of these changes, especially in the heterosexual population. Earlier in the epidemic, in the late 80s, the people requesting HIV tests were largely IDUs, who could only get free and confidential HIV testing at these centres. Both the absolute number and the proportion of IDUs coming for tests has decreased drastically in the later period due to both the reduction of people injecting drugs may be related to detailed Spanish harm reduction policy and its changes overtime [7, 18] but also to the increased availability of HIV testing sites. Also, it is likely that the HT coming for HIV tests in the early years also perceived themselves, and were, at higher risk for HIV infection. This may well be the case of the heterosexual women of the late 80s to mid 90s.

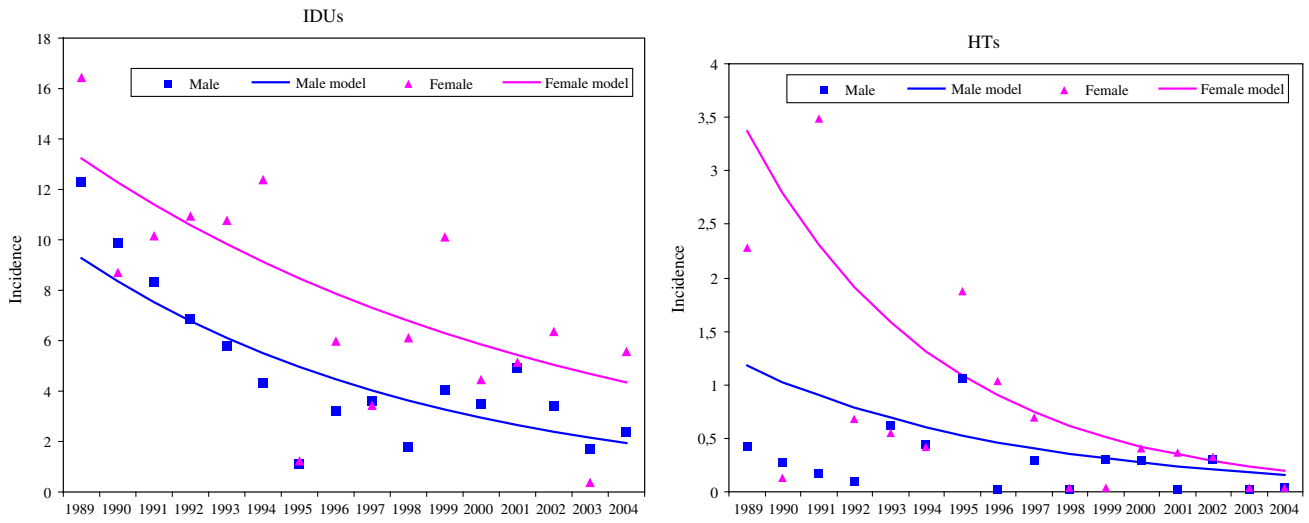

Fig. 2 HIV incidence trends by sex in IDUs and HT (×100 persons-year) attending the CIPS between 1989 and 2004. Joinpoint regression fitted

Although we do not have those data, it is highly likely that the heterosexual women of the earlier periods were the sexual partners of male IDUs and their high incidence rates in this early period represents the secondary HIV epidemic described by others in the past. As described by Des Jarlais, in areas with high HIV rates in IDUs, these have become the source for the secondary heterosexual epidemics in women [19]. Also females are very dependent on their males IDU partners for their own drug consumption and are often on a much weaker position with much more sharing of partners injecting equipments and paraphernalia [20].

The high initial prevalence rates reflect, as we have previously published, the detection of previously undiagnosed HIV infections in people, mainly IDUs, that had no change to access free and confidential HIV testing. In this sense, this prevalence reflects a period prevalence rather than serial HIV prevalence and needs to be interpreted differently. However, in spite of this detection bias and the selection biases discussed above, the declines in HIV prevalence are likely to reflect that HIV prevention messages and strategies in the population are having an effect. For HIV incidence, the decreases may also reflect the interventions carried out at these centres and provide evidence that counselling directed to people at risk for HIV is also having an impact, coinciding with the decline of HIV serial prevalence reported by Barrasa et al. in all transmission categories [8, 21].

To conclude, we have detected an increased vulnerability for HIV infection in women in a country whose HIV epidemic was largely driven by IDUs and where the proportion of women among people living with HIV has been low. Our results highlight the need to implement a gender perspective in future research and intervention programmes for HIV in our setting [22, 23].

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Authorship: I. Hurtado, designed the study, I Hurtado and S Pérez-Hoyos carried out the statistical analysis. I. Alastrue, C. Santos and T. Tasa were responsible for the recruitment and data collection. S. Pérez-Hoyos set up the original study and collaborated in its design. I. Hurtado, S. Pérez-Hoyos and J. Del Amo wrote and interpreted the results. All the authors revised the different versions of the manuscript.

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