HIV, HSV-2 and syphilis among married couples in India: patterns of discordance and concordance

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ABSTRACT

Objectives Differences in sexual networks probably explain the disparity in the scale of HIV epidemics in sub-Saharan Africa and India. HIV and sexually transmitted infection (STI) discordant couple studies provide insights into important aspects of these sexual networks. The authors quantify the role of male sexual behaviour in HIV transmission in married couples in India.

Methods The authors analysed patterns of HIV and STI discordance in married couples from two community surveys in India: the National Family Health Study-3 for HIV-1 and the Centre for Global Health Research health check-up for HSV-2 and syphilis. A statistical model was used to estimate the fraction of infections introduced by each of the two partners.

Results Only 0.8%, 16.0% and 3.5% of couples were infected (either partner or both) with HIV-1, HSV-2 and syphilis, respectively. A large proportion of infected couples were discordant (73.0%, 56.3% and 84.2% for HIV-1, HSV-2 and syphilis, respectively). This model estimated that, among couples with any STI, the male partner introduced the infection the majority of the time (HIV-1: 85.4%, HSV-2: 64.1%, syphilis: 75.0%).

Conclusions Male sexual activity outside of marriage appears to be a driving force for the Indian HIV/STI epidemic. Male client and female sex worker contacts should remain a primary target of the National AIDS Control Program in India.

INTRODUCTION

Theoretical analysis of HIV type 1 epidemiology indicates that a prerequisite for a generalised (ie, high prevalence) HIV epidemic in a community is strong connectivity of its sexual network.[1 2] With the exception of the Likoma Island Study,[3] sexual networks are rarely observed directly, and most studies are restricted to the behaviour and serostatus of network 'nodes', that is, to the sexually active individuals in the community. This lack of information on network structure, and the transmission that occurs within these networks, fuels debate about the importance of certain aspects of the network including concurrency and transactional sex.[4] Of particular interest is a better understanding of the differences in sexual networks between countries with generalised epidemics, notably in sub-Saharan Africa (SSA), and those with concentrated epidemics occurring elsewhere, including India. In India, initial dire forecasts of the HIV epidemic were based on the presence of large numbers of sex workers, their clients and high sexually transmitted infection (STI) prevalence in both groups.[5]

In view of these uncertainties regarding sexual networks, studies on transmission itself are important. Studies of couples in stable partnerships can provide important insights into factors that affect transmission. Both cross-sectional studies of infected couples as well as prospective cohort and intervention studies on HIV discordant couples have been important sources of information on HIV transmission and its determinants.[6] Cross-sectional studies on (discordant or concordant) infected couples are the simplest to carry out and several have been published to date, most of them from Africa, including several based on nationally representative demographic and health surveys.[7] One significant insight provided by these studies is that, in high-HIV prevalence African countries, a large percentage of HIV-infected couples are discordant. This suggests low transmission risk in stable partnerships. The risk of transmission between partners in a discordant couple in SSA may be lower than estimated from the prevalence of concordant HIV-positive couples, as many concordant couples have not been infected by each other but through sexual activity outside the partnership.[8] Until recently, it was widely believed that male sexual activity outside of marriage, either transactional or otherwise, is the primary driving force behind the large epidemics seen in many African countries,[9] a belief based primarily on self-reported sexual behaviour. Research in SSA suggests that men are only slightly more likely than women to bring the infection into the partnership, perhaps partly related to widespread long-term separation of spouses due to labour migration.[10–12] These new insights have provided clues for improving, and better targeting, interventions in SSA. Elsewhere, little is known about the precise role of outside relationships in creating discordant partnerships and the process of making them HIV concordant.

In India, few studies on discordant couples have been published.[13–16] None of these studies were conducted on population-representative samples; these studies were mostly conducted by testing partners of HIV-positive voluntary counselling and testing centre patients, and are therefore prone to selection bias. Nevertheless, these studies suggest that the African pattern, where both partners in a stable union are roughly equally likely to introduce HIV into the relationship, may not hold for India.[17] In one study (which gave few details on enrolment), 394 of the 457 uninfected partners were women, while in the other two studies, where couples were recruited from a voluntary counselling and testing centre, 35 of 42 and 966 of 996, respectively, uninfected partners were women. If these numbers reflect nationwide patterns, this suggests that in India, unlike in Africa, men are much more likely to introduce HIV in the partnerships than women. This would have implications for understanding the HIV epidemic in India, especially why HIV prevalence never reached 'African' levels. To explore this further, we calculated patterns of HIV discordance/concordance in married couples from the National Family Health Survey-3 (NFHS-3).[18] As all STIs are transmitted along the same networks, we also analysed discordance of two other STIs, HSV-2 and syphilis, both measured in another community survey, the Centre for Global Health Research (CGHR) health check-up survey.[19]

METHODS

Design

This study involves a cross-sectional analysis of sero-survey data and statistical modelling of patterns of HIV/STI discordance.

Setting

The setting for this study was the general population of India in 2006.

Participants

Our data came from population-based sero-surveys of the general population of India. Population-based survey data on couples (including biological measures of HIV, syphilis and HSV-2) were available from two sources: the NFHS-3 (n=26 230 couples) and the CGHR health check-up (n=543 couples), which were both conducted in 2006.[18 19] Data on HSV-2 and syphilis status of individuals in married cohabitating couples were available from the CGHR health check-up data. Data on the HIV status of married cohabitating couples were available from the NFHS-3. Estimates of male-to-female and female-to-male HIV, HSV-2 and syphilis transmission rates were available from the published literature.[20–23]

National Family Health Survey-3

The NFHS-3 is a nationally representative demographic household survey of Indian women (and their husbands if they are married). The survey focused on family health and health system usage, but also included an HIV testing component on a subset of participants. Interviews were conducted with 124 385 women aged 15–49 years and 74 369 men aged 15–54 years from all 29 states. Nationally, 102 981 women and men were tested for HIV. The NFHS-3 provides estimates of HIV prevalence for adult women and men at the national level, for Uttar Pradesh, and for five high HIV prevalence states (Andhra Pradesh, Karnataka, Maharashtra, Manipur and Tamil Nadu).

HIV testing in the NFHS-3

All HIV data in these analyses were from the NFHS-3 survey. All consenting women and men in households selected for the NFHS-3 were eligible for anonymous HIV testing. For 26 230 married couples, both the husband and the wife agreed to be tested for HIV in NFHS-3. Dried blood spots (DBSs) were collected from consenting women aged 15–49 years and men aged 15–54 years. Full details on the methods of collection, DBS management and HIV testing quality control are available in the NFHS-3 report.[18 24]

CGHR health check-up

All HSV-2 and syphilis data used in our study were from the CGHR health check-up. The CGHR health check-up is a comprehensive health survey of 2496 adults conducted in 2006 by trained male and female field workers in local languages.[19] The survey included a sexual behaviour component and a DBS sample was collected. The study was conducted in six sites in two states (Andhra Pradesh and Karnataka) and one union territory (Chandigarh) of India. The six sites were Sample Registration System units (randomly selected units representative—based on the 1991 census—of urban and rural areas at the state level for the collection of mortality and fertility data in India).[25] Surveyed households within each Sample Registration System unit were drawn from the 2001 India census. To maximise recruitment and participation, at least three visits to each household were made by the field workers. Details of demographic, socioeconomic, lifestyle characteristics (diet, cooking habits, exercise), basic medical parameters (blood pressure, height, weight), medical information (health status, disease conditions), alcohol and tobacco consumption were collected in a private area within the household. Sexual behaviour information was collected from participants between the ages of 18 and 49 years.

HSV-2 and syphilis testing in the CGHR health check-up

Six DBSs were collected from each individual on custom designed Whatman 3MM paper. At the end of the interview, each respondent received a health report card and a manual on basic health information. The DBS samples were dried for ~15 min in the field and then shipped at 4°C to the local state labs where they were checked for quality, recorded and further dried for 1–2 h and stored at −20°C. The DBS samples were tested for HSV-2 using the type-specific test, HSV-2 gpG2 IgG EIA (Focus HerpesSelect-2 type).[26] Trepanostika TP recombinant (BioMerieux Diagnostics, Marcy l'Etoile, France[27]) test was used to detect *Treponema pallidum* specific IgM and IgG antibodies in the samples.

Statistical analyses

We conducted an observational study of HIV transmission between couples. We constructed a statistical model of patterns of concordance and discordance of HIV, HSV-2 and syphilis among married cohabitating couples in the NFHS-3 and CGHR health check-up studies using cross-tabulations and stratification. Using unweighted frequencies of couples in each survey by STI status and an estimate of the ratio of female-to-male to male-to-female transmission risk for each STI as inputs, our model estimated two parameters: risk of male-to-female transmission for each STI and the proportion of infected couples in which the male was the first infected partner. Jackknife variance estimation was used to calculate 95% CIs for each of these parameters.[28] We used a χ^2 criterion minimisation approach to estimate parameters. Results were largely unaffected by ignoring sampling weights.

Details of the methods are given in the online supplementary appendix and are similar to those published previously.[23] Unlike the previously published method, we attempted to account for under-representation of HIV-positive concordant couples due to increased death, divorce and separation.

RESULTS

Characteristics of the HIV, HSV-2 and syphilis discordant and concordant couples from the NFHS-3 and CGHR health check-up surveys are shown in table 1. STI positivity is denoted by a subscript '+' symbol.

Of the 200 HIV-infected couples, 146 (73.0%) were discordant, and in 121 (82.9%) of these the male was the infected partner. There was little difference in pattern of HIV infection between high HIV and low HIV prevalence states (high HIV prevalence states: $Male_+,Fem_+$=38 (27.3%), $Male_+,Fem_-$=85

Table 1 Characterisation of study couples by STI concordance/discordance status

	Couple's STI status							
	Concordant negative		Concordant positive		Discordant female positive		Discordant male positive	
	Fem − | Male −		Fem + | Male +		Fem + | Male −		Fem − | Male +	
STI/variable	Mean/%	*SD*	Mean/%	*SD*	Mean/%	*SD*	Mean/%	*SD*
HIV n*:	**26 030**		**54**		**25**		**121**	
Age (wife—years)	31.6	*8.0*	29.7	*5.7*	31.4	*8.0*	30.6	*7.2*
Age (husband—years)	37.1	*8.4*	35.7	*6.2*	37.2	*9.4*	36.4	*7.1*
Muslim (%)	11.6		3.7		4.0		7.4	
Husband's literacy (%)	70.6		61.1		52.0		70.5	
Wife's literacy (%)	52.0		46.3		44.0		54.1	
Duration of marriage (years)	12.8	*8.3*	11.3	*6.8*	12.3	*8.6*	11.6	*7.2*
HSV-2 n:	**456**		**38**		**26**		**23**	
Age (husband—years)	42.1	*12.7*	47.1	*14.9*	48.3	*12.9*	46.2	*13.9*
Age (wife—years)	35.7	*11.2*	41.6	*15.2*	41.2	*11.5*	38.9	*12.4*
Husband's literacy (%)	84.0		84.0		81.0		83.0	
Wife's literacy (%)	67.0		42.0		46.0		55.0	
Syphilis n:	**524**		**3**		**4**		**12**	
Age (husband—years)	42.7	*12.9*	56.3	*2.3*	59.8	*14.6*	41.7	*11.7*
Age (wife—years)	36.4	*11.7*	46.7	*5.8*	44.8	*10.8*	36.2	*11.2*
Husband's literacy (%)	84.0		67.0		50.0		100.0	
Wife's literacy (%)	64.0		33.0		25.0		58.0	

*n, number of couples (unweighted counts).
Fem − | Male −, female negative male negative; Fem − | Male +, female negative male positive; Fem + | Male −, female positive, male negative; Fem + | Male +, female positive, male positive; HSV, herpes simplex virus; STI, sexually transmitted infection.

(61.2%), $Male_-,Fem_+=16$ (11.5%); low HIV prevalence states: $Male_+,Fem_+=16$ (26.2%), $Male_+,Fem_-=36$ (59.0%), $Male_-,Fem_+=9$ (14.8%)). The pattern in (high HIV) Manipur state, where intravenous drug use is common and may account for some of the infections in our sample, was also similar ($Male_+,Fem_+=12$, $Male_+,Fem_-=17$, $Male_-,Fem_+=2$). Also, there was no statistically significant difference in the pattern between urban and rural areas (data not shown). Overall HIV prevalence among couples in the NFHS-3 study was low, with only 200 (0.76%) out of 26 230 couples infected. Among the 52 314 individuals in these partnerships, this prevalence is even lower with only 254 (0.49%) partners testing HIV positive.

Religion (Muslim) was included as a proxy for male circumcision for couples from the NFHS-3 survey. Muslims were underrepresented among HIV-positive couples. Among concordant HIV-negative couples, 11.6% were Muslims while among HIV-positive couples the proportion of Muslim couples ranged from 3.7% to 7.4%. Less than 2% of couples in the CGHR health check-up sample were Muslim and religion was therefore omitted from our tables. We also omitted self-reported non-regular partners in the past 12 months, as none of the women in infected couples and only three men (discordant, male positive) reported such partners. Under-reporting of lifetime sexual partners was also suggested by our data as 91 of 121 (74.6%) HIV-positive serodiscordant men reported only one lifetime sex partner, as did 22 of 25 (88.0%) HIV-positive serodiscordant women. There were no statistically significant differences in number of lifetime births between the four concordancy/discordancy groups after adjustment for age (details not shown).

There were no differences in the duration of marriage between couples of different HIV status. The proportion of HIV-positive discordant couples did not change when restricted to one marriage with a duration of greater than or equal to 10 years (data not shown) suggesting that most HIV infections occurred during marriage instead of before.

Among couples in the NFHS-3 survey, husbands were approximately 6 years older than their wives and this pattern held across HIV status strata and was generally true across HSV-2 and syphilis strata as well.

Parameter estimates from our statistical model, used to assess which partner introduced HIV into the partnership, are shown in table 2.

Among HIV-infected couples, our model estimated that the male partner introduced the infection 84.2% (95% CI 78.5% to 89.9%) to 88.9% (95% CI 84.7% to 93.1%) of the time depending on the ratio of transmission risks and the assumed effect of excess mortality and separation due to infection on the number of concordant cases. Similarly, among syphilis-infected couples, our model estimated the male partner predominantly introduced the infection, that is, 72.0% (95% CI 48.6% to 95.5%) to 76.9% (95% CI 56.3% to 97.4%) of the time, depending on our assumptions of the ratio of female-to-male to male-to-female transmission risks (0.5–2). Among HSV-2-infected couples, the fraction of couples in which the male partner introduced the infection was more sensitive to the assumption of ratio of transmission risks as this measure varied from 56.9% (95% CI 43.6% to 70.3%) to 67.3% (95% CI 56.7% to 77.8%). Numbers of couples with syphilis infection were too small to generate precise estimates of the risk of male-to-female transmission probabilities. State-stratified analyses were not possible due to small numbers of HIV-positive couples.

DISCUSSION

As suggested by earlier discordancy studies from India, we found that men were more likely than their female partners to introduce HIV in the relationship among couples included in the NFHS-3. The same appeared to hold true for syphilis, but less so for HSV-2 even when much higher male-to-female than female-to-male transmission rates were assumed; perhaps due to low specificity of the HSV-2 test as was also observed in South Africa.[29] The percentage (73.0%) of HIV discordance among infected couples in the NFHS-3 was similar to those found in SSA demographic and health surveys carried out in five African countries (ie, 66.7%–85.2%).[7] This similarity is surprising as

Table 2 Fractions of HIV, HSV-2 and syphilis infections among infected couples originating from the husband

STI†	Fem+ | Male −	Fem − | Male +	Fem + | Male +	Number of infected couples N	Ratio of transmission risks (female-to-male to male-to-female) r	Inflation factor for excess mortality and divorce rates in concordant couples (HIV only) q	Risk of male-to-female transmission of STI p (95% CI)	Fraction of infected couples in which the male was the first infected partner* f (95% CI)
HIV	25	121	54	200	0.25	1	30.0% (23.2% to 36.9%)	86.5% (81.5% to 91.5%)
					0.50	1	29.1% (22.5% to 35.7%)	85.4% (80.0% to 90.7%)
					0.75	1	28.1% (21.7% to 34.5%)	84.2% (78.5% to 89.9%)
					0.25	1.2	34.0% (26.9% to 41.2%)	87.0% (82.2% to 91.9%)
					0.50	1.2	33.1% (26.0% to 40.2%)	85.8% (80.6% to 91.0%)
					0.75	1.2	32.0% (25.1% to 38.9%)	84.4% (78.8% to 90.0%)
					0.25	2	46.4% (38.3% to 54.5%)	88.9% (84.7% to 93.1%)
					0.50	2	45.4% (37.4% to 53.4%)	87.3% (82.5% to 92.0%)
					0.75	2	44.1% (36.2% to 52.1%)	85.3% (79.9% to 90.7%)
HSV-2	26	23	38	87	0.143	1.000	60.7% (48.2% to 73.2%)	67.3% (56.7% to 77.8%)
					0.286	1.000	58.7% (46.2% to 71.3%)	64.1% (52.6% to 75.6%)
					0.571	1.000	53.6% (41.2% to 65.9%)	56.9% (43.6% to 70.3%)
Syphilis	4	12	3	19	0.500	1.000	17.9% (0.0% to 36.9%)	76.9% (56.3% to 97.4%)
					1.000	1.000	15.8% (0.0% to 32.8%)	75.0% (52.8% to 97.1%)
					2.000	1.000	12.3% (0.0% to 25.3%)	72.0% (48.6% to 95.5%)

Number of observed concordant HIV-infected couples for HIV was multiplied by 1, 1.2 and 2, respectively, to take into account a possible, but uncertain, excess mortality among these couples compared with HIV discordant couples.
The parameters r and q, as well as the numbers of the three types of infected couples are inputs, while p and f are estimated using our model.
*Summary of results from weighted data from NFHS-3: HIV (q=1, range of f= 82.2−85.2); HIV (q=1.2, range of f=82.2−85.7); HIV (q=2, range of f=82.2−87.4).
†HIV data from NFHS-3; HSV-2 and syphilis data from CGHR SRS health check-up; each row in the table is a separate model fit. Only the last two columns (p, f) are model outputs.
CGHR, Centre for Global Health Research; f, fraction of infected couples in which the male was the first infected partner; Fem − | Male +, female negative male positive; Fem + | Male −, female positive, male negative; Fem + | Male +, female positive, male positive; HSV, herpes simplex virus; N, number of infected couples; NFHS-3, National Family Health Survey-3; p, risk of male-to-female transmission of STI; q, inflation factor for excess mortality and divorce rates in concordant couples (HIV only); r, ratio of transmission risks (female-to-male to male-to-female); SRS, Sample Registration System; STI, sexually transmitted infection.

HSV-2, an established HIV transmission cofactor in both India and SSA, is much less prevalent in India than in SSA.[27] Unfortunately, as NFHS-3 did not test for HSV-2 status we could not explore the role of this coinfection in greater detail. Perhaps lower levels of HSV-2 in India were offset by the lower levels of—protective—male circumcision in India (approximately 12% of the total male population) than in Africa.

We estimated that a sizable minority of 10%–20% of HIV infections in India are introduced by the female partner. These results appear to agree roughly with data from a nationally representative sexual behaviour survey conducted in 2006 in the general population where 5.2% of married men reported a non-regular partner during the past year compared with 1.7 % of married women.[30] Unfortunately, it was not possible to corroborate this estimate with data on self-reported non-regular and lifetime partners from NFHS-3 itself, as these were grossly under-reported by both men and women. Under-reporting of the number of non-regular and lifetime sexual partners in household surveys was also evidenced by HSV-2 (2.4%) and syphilis (1.2%) prevalence among women in the CGHR health check-up reporting never having had sex.[19] The imbalance in male-to-female and female-to-male transmission also demonstrates both the strengths and limitations and the biases of a family-based survey as a tool in understanding sexual network structures. As (in heterosexual transmission) all HIV-positive men have been infected by HIV-infected women and vice versa, it is clear that this family-based survey misses most female-to-male transmissions, presumably because much of this transmission takes place during transactional sex, which is not captured by family-based surveys. Our study had other limitations. The statistical model needs assumptions about the impact of HIV on the dissolution of couples, a parameter for which few data are available. Furthermore, given the cross-sectional nature of the data, we were unable to estimate a per-year transmission risk. The relatively small number of HIV-positive couples precluded state-specific analyses, despite likely heterogeneities in a country the size of India. Future analysis could incorporate state-level analyses to account for regional variation in the drivers of HIV transmission in India.[31]

Other research supports our findings that male sexual activity outside of stable partnerships, presumably via transactional sex with sex workers, is a driving force for the heterosexual epidemic in India. A nationally representative behavioural surveillance survey of the general Indian population conducted in 2006 showed that a large proportion of men's self-reported non-regular partners are sex workers, especially when men report more than one such partner in the past 12 months.[32] Our findings are also supported by modelling work of the epidemic in south India where it was estimated that greater than 90% of incident HIV/HSV-2 infections among the general male population resulted directly from commercial sex work and among the general female population 80%–90% of these infections resulted from bridging infections from clients of female sex workers (FSWs).[33] The insight into the role of commercial sex work is important for mathematical models that are used to explain and predict the HIV epidemic in India.[34] The importance of male sexual activity outside of marriage also appears to explain why HIV prevalence in India is higher in men than in women[18] and provides support to current efforts by both the Government of India and non-governmental organisations to reduce risk in FSW–male client contacts. Indeed, understanding these sexual network characteristics may help explain the

Key messages

- ► There is a high prevalence of discordance among HIV-infected couples in India (73%).
- ► The majority of HIV-infected couples were likely to be first infected by the male partner.
- ► Interventions to prevent transmission within HIV discordant couples should be pursued; however, male client–female sex worker contacts should remain the focus of prevention.
- ► There is evidence of under-reporting of sexual risk behaviour in general population surveys but the inclusion of sexually transmitted infection biomarkers can provide key insights into transmission networks.

recently observed declines in HIV prevalence among young antenatal women in south India.[35–37] Nevertheless, key remaining gaps in knowledge include: how many first infections in HIV-infected couples were acquired prior to partnership formation versus during the partnership as well as how many concordant HIV-positive partnerships arose as a result of sexual activity outside or within partnership transmission. These gaps call for caution in interpreting our results. Clearly, there is a need for long-term follow-up studies similar to the Partners study carried out in various African countries.[12]

While targeted interventions may be important in controlling HIV in India, they do not directly address the needs of uninfected female partners of infected men. The high prevalence of HIV discordance in HIV-infected couples suggests that there is opportunity for HIV prevention among HIV-positive persons in relationships. HIV prevention efforts in India are generally not targeted at couples and partners of HIV-infected persons are at risk of infection. Addressing this need should be made a priority.[6 38]

Disclosure The views expressed herein are those of the authors and do not necessarily reflect the official policy or position of The Bill & Melinda Gates Foundation.

Competing interests None.

Ethics approval Ethical clearance for the study was obtained from the Health Ministry Screening Committee of the Indian Council of Medical Research and the Institutional Review Boards of the participating institutions (Nizam's Institute of Medical Science, St John's National Academy of Health Sciences, IERB/177/05, and Post Graduate Institute of Medical Education and Research). Written informed consent was obtained from all participants.

Contributors PA, NN and SKS were responsible for study design; SKS, RK, ND and PJ oversaw the study implementation for the CGHR health check-up; PA and NN wrote the manuscript and supervised all analyses; PA managed the database; PA and NN conducted the statistical analyses; All authors reviewed the manuscript and provided substantive comments.

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