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Prevalence and correlates of Herpes Simplex Virus-2 and syphilis infections in the general population in India

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ABSTRACT

Objectives To determine the prevalence and correlates of Herpes Simplex Virus-2 (HSV-2) and syphilis infections in the general population in India.

Methods 2456 adults were surveyed in Hyderabad, Bangalore and Chandigarh in India. Socio-demographic and lifestyle characteristics were obtained through a questionnaire, and a dried blood spot (DBS) was collected from all individuals aged 18 years and over; sexual behaviour was collected from those aged 18–49 years. DBS samples were tested for HSV-2 and syphilis serology. The association between HSV-2 and syphilis infections with socio-demographic and behavioural variables was analysed using multivariable logistic regression.

Results The prevalence of HSV-2 and syphilis was 10.1% and 1.7%, respectively. Geographic differences in HSV-2 prevalence were significant, while for syphilis it was comparable. Urban–rural differences in prevalence were only seen for syphilis. For both infections, the prevalence between males and females was not significantly different. In males and females, HSV-2 prevalence increased significantly with increasing age; for syphilis, a slight trend was seen only in females. In a multivariable analysis, HSV-2 infection in males and females was associated with site, religion and testing positive for syphilis, in addition to reporting ≥2 lifetime partners in the previous year among males and being ever married or having had sex with a non-regular partner in the last year among females.

Conclusions The burden and geographic heterogeneity of HSV-2 and syphilis infections in India are significant. A national household and DBS-based sexually transmitted infection (STI) surveillance system would enable monitoring, especially in relation to the HIV epidemic, and planning of evidence-based prevention and treatment programmes.

INTRODUCTION

According to WHO estimates, 15% (50 million) of the 340 million new annual sexually transmitted infection (STI) cases are in India, and 44% (151 million) in South and South-East Asia.[1] STIs that cause genital ulcer disease (GUD) in particular, such as Herpes Simplex Virus-2 (HSV-2) and syphilis, have gained significant attention in recent years as observational studies have associated both infections with increased risk of HIV in addition to causing significant morbidity.[1–8] HSV-2 is the leading cause of GUD in developing countries.[1] Since HSV-2 prevalence is not influenced by changes in service provision or treatment, its transmission dynamics parallels that of HIV, and epidemiological evidence supports the strong association between HSV-2 and HIV infections, the population prevalence of HSV-2 can be used as a reliable proxy for risk for HIV infection. Furthermore, to overcome the self-reporting and social desirability bias often found in behavioural surveys, the prevalence of STIs such as HSV-2 and syphilis could be used as serological markers for patterns of sexual behaviour within populations.[9 10]

HSV-2 is one of the most prevalent STIs in the world.[11 12] While the prevalence of syphilis has been generally declining since the introduction of antibiotics, outbreaks still occur, especially in high-risk groups.[6 13] Both STIs show significant variability in prevalence by population group and geography. Data from India on syphilis and HSV-2 prevalence are sparse and varied. Reported HSV-2 prevalence varies between 1.0% and 18.9% from general population-based surveys,[14–21] between 9.7% and 83% from STD clinics,[22–24] and between 2.0% and 79.0% from high-risk group surveys.[25–28]

We conducted a cross-sectional population-based survey in three cities (Hyderabad in the state of Andhra Pradesh, Bangalore in the state of Karnataka, and Chandigarh) in India to determine the prevalence and predictors of HSV-2 and syphilis in the general population. Compared with other general population studies conducted in India to date, our sample size was one of the largest and most geographically diverse.

METHODS

Study sites

The study was conducted in 2006 at two sites each in Bangalore, Hyderabad and Chandigarh in India. The six sites were Sample Registration System (SRS) units, which are randomly selected units representative of urban and rural areas at the state level for the collection of mortality and fertility data.[29] Two SRS sites were purposively chosen to be located close to the three coordinating city centres, with one site in a low-income urban area and the second site in a periurban rural area. Surveyed households within each SRS unit were drawn from the 2001 India census. Listing of the existing households was provided by the local Directorate of Census Operations for the state.

Study design

The survey was designed as a comprehensive health check-up survey and conducted by male and female

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field workers in local vernacular. Field workers were trained and certified by a central team in interviewing techniques, questionnaire administration, obtaining physical measurement and dried blood spot (DBS) collection. In each household, all individuals aged 18 years and above were invited to participate. All literate participants were provided with an information sheet detailing the objectives of the study and inviting their participation in English and local vernacular. For illiterate participants, a literate member of the community explained the survey. To maximise participation, at least three home-visits were made by the field workers to each household. Socio-demographic, lifestyle characteristics (diet, cooking habits, exercise), basic medical parameters (blood pressure, height, weight), medical information (health status, disease conditions), alcohol and tobacco consumption, and sexual behaviour factors (from participants between the ages of 18 and 49 years) were collected in a private area within the household whenever possible. Blood was collected in the form of DBS from all participants. Six bloodspots were collected from each individual on custom-designed Whatman No 3 paper. At the end of the interview, each respondent received a health report card and a health information brochure. 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. For serological testing, DBS cards were shipped to the microbiology laboratory at Nizam's Institute of Medical Sciences in Hyderabad. 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.

Serological testing for HSV-2 and syphilis

The DBS samples were tested for HSV-2 IgG antibodies using a type-specific test (HerpesSelect 2 ELISA IgG, Focus Technologies, Cypress, California).[30] The Trepanostika TP recombinant (BioMerieux-diagnostics) test was used to detect *T pallidum* specific IgM and IgG antibodies in the samples. Both tests measure lifetime exposure to pathogens. When compared with serum samples, both tests showed comparable specificity and sensitivity with DBS, and have been validated in the Indian population.[31]

Statistical analysis

The data were analysed using STATA statistical package, version 10.0 software. Data for women and men were analysed separately. First, the association between HSV-2/syphilis status and each socio-demographic or sexual behaviour variable was examined with univariate logistic regression. Second, the association between each demographic or sexual behaviour variable and STI outcome was recalculated adjusting for age in years and study site only, as both were strongly associated with STI outcomes. Third, a multivariable logistic regression model was constructed using backward elimination.[32] Age as a continuous variable and site were put into the model a priori. Independent variables were grouped in two hierarchical levels or blocks. The first hierarchical level comprised all socio-demographic variables that were associated with HSV-2 in the unadjusted analysis (which we refer to as 'distal' factors). The second hierarchical level further comprised two strata (which we refer to as 'proximal' factors): (a) non-sexual behavioural and (b) sexual behviour variables. Sexual behaviour questions were only asked of a subset (n=1848, 78.7%) of study participants. Independent variables were grouped into these blocks because we hypothesised that distal and proximal factors would affect STI risk via different mechanisms. Variables were retained in the model if regression coefficients reached a p value of less than or equal to 0.2 or if their removal resulted in a change of over 10% in the OR of another variable. The final model was constructed using only retained distal and proximal variables, and evaluated the association between the retained variables and STI outcomes.

RESULTS

Study participants

From the 2001 census, a total of 3659 adults aged 18 years and older were listed as residents of the six SRS units surveyed. By 2006, 513 (14.0%) adults had migrated out of the units. Of the 3146 resident adults, 2456 (78.1%) participated in the survey. A total of 2347 (95.6%) participants also agreed to give DBS samples. Sexual behaviour information was collected from 1848 participants (883 males and 965 females) between the ages of 18 and 49 years in addition to the other survey components. Of the 690 (21.9%) eligible adults who did not participate in the survey (non-responders), 152 (22.0%) refused to participate, and 538 (88.0%) were not reachable.

Socio-demographic characteristics of responders and non-responders

Online supplementary table 1 compares the socio-demographic characteristics of responders (individuals who completed the questionnaire and gave a DBS sample) and non-responders (individuals who did not participate in the survey). Overall, females were more likely to respond than males ($p<0.01$). Among both sexes, higher response rates were seen among Chandigarh residents. Among males, response rate was higher among those between the ages of 55 and 64 years or educated and lower among those between the age of 35 and 44 years or illiterate. Among females, the response rate was higher among those who were graduates and lower among those who were 65 years of age or older. Response rate was not associated with marital status or urban–rural residence among both sexes.

Prevalence and determinants of HSV-2 and syphilis infection in India

The overall prevalence of HSV-2 and syphilis was 10.1% (95% CI 8.9% to 11.4%) and 1.7% (CI 1.1% to 2.2%), respectively. However, HSV-2 prevalence showed significant geographic variation in India. Prevalence of HSV-2 was significantly higher in Hyderabad (17.8%; CI 15.0% to 20.6%) than in Bangalore (5.8%; CI 4.1% to 7.5%) or Chandigarh (7.5%; CI 5.7% to 9.2%) ($p<0.00$). The geographic variation in the prevalence of syphilis was not significant (Bangalore: 1.9%; CI 0.9% to 2.9%; Hyderabad: 1.9%; CI 0.9% to 2.9%; Chandigarh: 1.2%; CI 0.5% to 2.0%) ($p=0.47$). Differences between males and females in the overall prevalence of HSV-2 (8.9% vs 11.3%; $p=0.06$) and syphilis (2.0% vs 1.3%; $p=0.18$) were not statistically significant. While the prevalence of HSV-2 was not significantly different between urban and rural areas (urban, 8.9%; rural, 10.8%; $p=0.15$), syphilis prevalence was higher in rural areas (urban, 0.9%; rural, 2.0%; $p=0.05$). 2.4% and 1.2% of the females who reported never having had sex were found to be HSV-2- and syphilis-positive, respectively.

In a univariate analysis conducted for males and females separately, several factors were associated with HSV-2 and syphilis infection (online supplementary table 2). Age was a significant

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determinant of infection with prevalence showing a strong increasing trend with age in both sexes ($p<0.001$) for HSV-2 and a slight trend in females (p value, 0.048) only for syphilis (figure 1A,B). In males and females, when compared with the grand mean, the prevalence of HSV-2 was significantly higher in Hyderabad and lower in Bangalore, while no difference in syphilis prevalence was seen by site. In both sexes, the odds of HSV-2 infection was higher among those who were ever married, Christian or illiterate, those who had completed only primary education, those drinking alcohol, positive for syphilis infection or ever had sex with a person of the opposite sex (online supplementary tables 2, 3). Furthermore, the prevalence of HSV-2 was significantly higher in males who resided in urban areas, or had sex with a man in the last year, and females who had sex with a non-regular partner in the last year (online supplementary table 3). Females who had their first sexual intercourse after 18 years of age were less likely to be HSV-2-positive, whereas the age of first-time sexual intercourse was not associated with HSV-2 infection in males.

In males, prevalence of syphilis was significantly higher among those who had been married, had completed primary education only, ever had an HIV test or were HSV-2 positive (online supplementary tables 2, 3). Prevalence of syphilis in females, on the other hand, was significantly higher among those who were illiterate, HSV-2 positive, or had sex with a non-regular partner in the last year.

Tables 1, 2 summarise the factors associated with HSV-2 and syphilis infection after adjusting for age and site. In an adjusted analysis, the relative odds of HSV-2 infection in both sexes increased with being Christian, Sikh or testing positive for syphilis. In addition, the likelihood of carrying HSV-2 antibodies in females remained associated with having been married and having had sex with a non-regular partner in the last year. In an adjusted analysis, syphilis infection was associated with being positive for HSV-2 in both sexes, having had an HIV test and smoking cigarettes in males and sex with a non-regular partner in the last year in females.

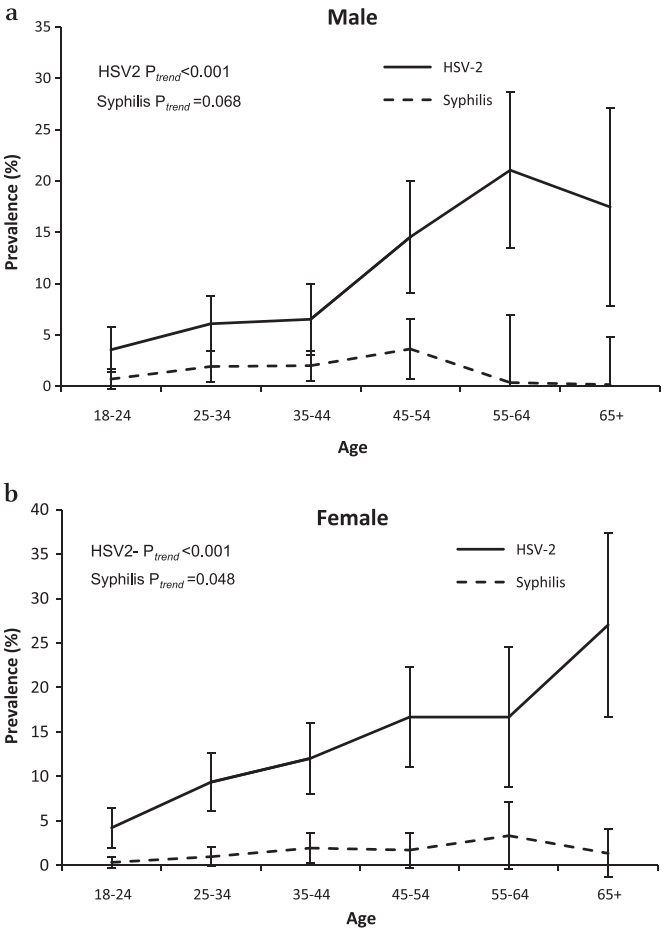

Figure 1 Agewise prevalence of Herpes Simplex Virus-2 (HSV-2) and syphilis.

Multiple logistic regression for HSV-2 and syphilis

Using key demographic and behavioural variables that were significant predictors, multivariable logistic regression models for HSV-2 and syphilis infection were constructed using backward elimination based on two hierarchical levels (see Methods).[32] However, due to the very small number of syphilis positive cases, the model was not powerful enough to determine associations and is not presented. We present the final HSV-2 multivariable model in table 3.

For males, the variables that remained in the first level of the model, which comprised socio-demographic variables, were age, site, religion and education. Controlling for age, religion, and education, males in Hyderabad had an increased odds of being HSV-2 positive compared with the grand mean. Religion remained an important predictor of HSV-2 infection in males when controlling for age, site and education. In the second level of the model, we first tested the association of HSV-2 infection in males with non-sexual behaviour factors including syphilis infection, alcohol consumption and smoking. In addition to the socio-demographic variables that were moved forward from the previous level, all three non-sexual behaviour variables remained in the model. When controlling the non-sexual behaviour variables for age, site, religion and each other, only syphilis infection remained associated with HSV-2 infection. Finally, we tested the association between HSV-2 infection and sexual behaviour variables (age at first sex, lifetime number of partners, non-regular partners in the last year) and ever had an HIV test. While all of the sexual behaviour variables, HIV test and socio-demographic variables that were moved forward remained in the model, only having two or more lifetime sexual partners was associated with HSV-2 infection in males.

A multivariable model, similar to that described for males, was also constructed for females. All of the socio-demographic variables that were included in the first level (age, site, religion, marital status and education) remained in the final model. Females had increased odds of being HSV-2 positive if Christian, Sikh, ever married, or living in Hyderabad, when the variables were controlled for each other in addition to education and age. When we tested the association between HSV-2 infection and non-sexual behaviour factors of syphilis infection or alcohol consumption, while both remained in the model, only syphilis infection was found to be an important predictor of HISV-2 infection. We then tested for the association between HSV-2 infection and the same sexual behaviour variables tested for in males while adjusting for socio-demographic variables moved forward from the previous level. For females, sex with a non-regular partner in the last year remained in the model and was found to be significantly associated with HSV-2 infection.

DISCUSSION

This study provides a profile of HSV-2 and syphilis infections in the general population in three geographic locations in India. While both STIs cause GUD, the prevalence and predictors are considerably different in India. Unlike syphilis, we found the prevalence of HSV-2 to be higher in Hyderabad compared with Bangalore and Chandigarh. This heterogeneity parallels that of

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Table 1 Prevalence and predictors of Herpes Simplex Virus-2 (HSV-2) and syphilis, N=2347 ages 18+ years

	Male (n=1134)				Female (n=1213)			
	HSV-2		Syphilis*		HSV-2		Syphilis	
Characteristic	Percentage positive (N)	OR† (95% CI)	Percentage positive (N)	OR† (95% CI)	Percentage positive (N)	OR† (95% CI)	Percentage positive (N)	OR† (95% CI)
Basic prevalence	8.9 (1134)		2.0 (1133)		11.3 (1213)		1.3 (1213)	
Area residence								
Urban	6.1 (359)	1.0	1.1 (359)	1.0	11.3 (398)	1.0	0.8 (398)	1.0
Rural	10.2 (775)	1.5 (0.9 to 2.5)	2.5 (774)	2.0 (0.7 to 6.2)	11.3 (815)	0.8 (0.6 to 1.2)	1.6 (815)	1.9 (0.5 to 6.8)
Marital status								
Never married	4.4 (341)	1.0	0.6 (341)	1.0	2.5 (163)	1.0	1.8 (163)	1.0
Ever married	10.8 (793)	1.1 (0.5 to 2.2)	2.7 (792)	3.8 (0.8 to 19.0)	12.7 (133)	3.2 (1.1 to 9.2)	1.2 (1050)	0.3 (0.1 to 1.3)
Religion								
Hindu	7.5 (935)	1.0	1.8 (934)	1.0	10.2 (995)	1.0	1.5 (995)	1.0
Muslim	6.3 (16)	1.1 (0.13 to 8.84)	0.0 (16)	NA NA	11.8 (17)	1.3 (0.3 to 6.1)	0.0 (17)	NA NA
Christian	33.3 (48)	4.3 (2.1 to 8.8)	4.2 (48)	2.4 (0.6 to 11.2)	28.0 (50)	2.4 (1.2 to 4.8)	0.0 (50)	NA NA
Sikh	10.1 (129)	2.3 (1.1 to 5.1)	3.1 (129)	3.2 (0.7 to 14.6)	13.5 (141)	2.3 (1.1 to 4.5)	0.7 (141)	0.6 (0.1 to 5.9)
Education								
Graduate	6.7 (721)	1.0	1.4 (721)	1.0	5.7 (494)	1.0	0.6 (494)	1.0
Primary	11.5 (269)	1.0 (0.6 to 1.6)	4.1 (269)	2.4 (1.0 to 6.2)	10.7 (243)	1.5 (0.9 to 2.8)	0.8 (243)	1.2 (0.2 to 7.7)
Illiterate	15.3 (137)	0.7 (0.3 to 1.3)	1.5 (136)	0.7 (0.1 to 4.0)	17.5 (468)	1.5 (0.9 to 2.7)	2.4 (468)	2.8 (0.6 to 14.0)
Alcohol consumption								
No	8.2 (728)	1.0	1.8 (727)	1.0	9.8 (1044)	1.0	1.3 (1044)	1.0
≤2 days per week	5.2 (211)	0.6 (0.3 to 1.1)	2.8 (211)	1.9 (0.7 to 5.1)	24.7 (81)	1.3 (0.7 to 2.4)	1.2 (81)	0.4 (0.1 to 3.6)
≥3 days per week	15.4 (156)	1.2 (0.7 to 1.2)	2.6 (156)	1.5 (0.5 to 5.0)	16.2 (37)	0.6 (0.2 to 1.6)	0.0 (37)	NA NA
Smoking bidis								
No	7.9 (719)	1.0	1.5 (718)	1.0	11.0 (1146)	1.0	1.2 (1146)	1.0
1–7 per day	9.2 (76)	0.9 (0.4 to 2.2)	4.0 (76)	2.5 (0.7 to 9.6)	0.0 (1)	NA NA	0.0 (1)	NA NA
8+ per day	13.8 (152)	1.0 (0.5 to 1.7)	1.3 (152)	0.7 (0.1 to 3.3)	0.0 (1)	NA NA	0.0 (1)	NA NA
Smoking cigarettes								
No	7.9 (719)	1.0	1.5 (718)	1.0	11.0 (1146)	NA NA	1.2 (1146)	NA NA
1–7 per day	9.8 (112)	1.4 (0.7 to 2.8)	4.5 (112)	3.1 (1.1 to 9.3)	0.0 (0)	NA NA	0.0 (0)	NA NA
8+ per day	6.1 (33)	0.5 (0.1 to 2.2)	6.1 (33)	3.6 (0.7 to 17.2)	0.0 (0)	NA NA	0.0 (0)	NA NA
Chewing tobacco								
No	8.9 (971)	1.0	1.9 (970)	1.0	11.2 (1063)	1.0	1.1 (1063)	1.0
Yes	8.9 (158)	1.4 (0.7 to 2.5)	3.2 (158)	1.5 (0.5 to 4.3)	12.5 (144)	0.6 (0.3 to 1.0)	2.1 (144)	1.1 (0.3 to 4.5)
Married men spent time away from home								
No	10.7 (737)	1.0	2.7 (737)	NA NA	NA NA	NA NA	NA NA	NA NA
Yes	10.2 (49)	1.3 (0.5 to 3.6)	0.0 (48)	NA NA	NA NA	NA NA	NA NA	NA NA
Did husband spend time away from home?								
No	NA NA	NA NA	NA NA	NA NA	12.2 (861)	1.0	1.3 (861)	NA NA
Yes	NA NA	NA NA	NA NA	NA NA	4.9 (61)	0.6 (0.2 to 2.0)	0.0 (61)	NA NA
Syphilis status								
Negative	8.4 (1110)	1.0	NA NA	NA NA	10.9 (1197)	1.0	NA NA	NA NA
Positive	34.8 (23)	5.9 (2.2 to 15.6)	NA NA	NA NA	37.5 (16)	3.6 (1.2 to 11.0)	NA NA	NA NA
HSV-2 status								
Negative	NA NA	NA NA	1.5 (1032)	1.0	NA NA	NA NA	0.9 (1076)	1.0
Positive	NA NA	NA NA	7.9 (101)	6.0 (2.3 to 15.5)	NA NA	NA NA	4.4 (137)	3.7 (1.3 to 11.1)

*Males tested for syphilis, n=1133.
†OR adjusted for age and site.
N, total number of individuals (positive and negative) in that category.

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Table 2 Prevalence and predictors of Herpes Simplex Virus-2 (HSV-2) and syphilis by sexual behaviour, subset analysis, aged 18–49 (N=1848)

	Male (n=883)				Female (n=965)			
	HSV-2		Syphilis		HSV-2		Syphilis	
Characteristic	Percentage positive (N)	OR* (95% CI)	Percentage positive (N)	OR* (95% CI)	Percentage positive (N)	OR* (95% CI)	Percentage positive (N)	OR* (95% CI)
Sex with a man in the last year (men only)								
No	6.3 (871)	1.0	1.6 (871)	1.0	NA NA	NA NA	NA NA	NA NA
Yes	33.3 (3)	10.1 (0.8 to 134.2)	0.0 (3)	NA NA	NA NA	NA NA	NA NA	NA NA
Ever had an HIV test								
No	6.6 (771)	1.0	1.3 (771)	1.0	9.5 (778)	1.0	0.0 (778)	1.0
Yes	2.3 (89)	0.3 (0.1 to 1.3)	4.5 (89)	3.5 (1.1 to 11.6)	9.8 (153)	1.3 (0.7 to 2.4)	1.2 (153)	NA NA
Ever had sex with opposite sex								
No	3.7 (272)	1.0	0.0 (272)	NA NA	2.4 (167)	1.0	1.2 (167)	1.0
Yes	7.5 (611)	1.1 (0.5 to 2.7)	2.3 (611)	NA NA	11.0 (798)	2.9 (1.0 to 8.3)	0.9 (798)	0.4 (0.1 to 2.5)
Of those who responded yes to sex with opposite sex								
	Male n=611				Female n=798			
Life time no of sex partners								
1	7.5 (452)	1.0	2.2 (452)	1.0	10.8 (780)	1.0	0.8 (780)	1.0
>=2	7.9 (152)	1.4 (0.7 to 3.0)	2.6 (152)	1.3 (0.4 to 4.2)	26.7 (15)	3.3 (0.9 to 11.2)	6.7 (15)	7.7 (0.8 to 70.8)
Sex with non-regular partner in the last year								
No	8.2 (491)	1.0	2.0 (491)	1.0	10.7 (784)	1.0	0.6 (784)	1.0
Yes	4.1 (49)	0.7 (0.2 to 3.0)	4.1 (49)	1.5 (0.3 to 7.4)	30.8 (13)	4.6 (1.2 to 16.8)	15.4 (13)	25.8 (4.2 to 157.2)
Ever paid for sex								
No	7.8 (576)	1.0	2.1 (576)	1.00	NA NA	NA NA	NA NA	NA NA
Yes	3.1 (32)	0.7 (0.1 to 5.6)	6.3 (32)	3.1 (0.6 to 16.0)	NA NA	NA NA	NA NA	NA NA
Age at first sex								
Mean (SD)	21.4 (4.5)	1.0 (0.9 to 1.1)	22.9 (4.5)	0.9 (0.9 to 1.1)	16.8 (2.9)	1.0 (0.9 to 1.1)	16.3 (2.4)	0.9 (0.7 to 1.2)
HSV-2 status								
Negative	NA NA	NA NA	1.8 (565)	1.0	NA NA	NA NA	0.6 (710)	1.0
Positive	NA NA	NA NA	8.7 (46)	9.5 (2.5 to 36.2)	NA NA	NA NA	3.4 (88)	5.9 (1.2 to 29.1)
Syphilis status								
Negative	7.0 (597)	1.0	NA NA	NA NA	10.8 (791)	1.0	NA NA	NA NA
Positive	28.6 (14)	9.4 (2.4 to 36.8)	NA NA	NA NA	42.8 (7)	5.9 (1.2 to 29.0)	NA NA	NA NA

N, total number of individuals (positive and negative) in that category.
*OR adjusted for age and site.

HIV prevalence in women attending antenatal clinics (Hyderabad 2.0%, Bangalore 1.3–1.5% and Chandigarh 0.25%).[33] This is likely to be because HIV and HSV-2 have similar transmission probabilities and suggests that the population prevalence of HSV-2 could be an important marker for HIV risk. As reported elsewhere, a significant association between age and HSV-2 prevalence was observed in both sexes.[34] A slight association in females only was observed for syphilis.

In an adjusted analysis for age and site conducted separately for males and females, correlates of HSV-2 infection included coinfection with syphilis, being Christian or Sikh (although marginal), having been married (females only) and high-risk sexual behaviour in the last year. For syphilis, correlates included being infected with HSV-2 (both sexes), having had an HIV test (males only) and sex with a non-regular partner in the last year (females only). An age- and site-adjusted index analysis was conducted for both HSV-2 and syphilis, and the correlates were found to be the same (data not shown). Using a multiple logistic regression analysis, common predictors of HSV-2 infection for males and females included being Christian, residing in Hyderabad and being syphilis-positive. Sex-specific predictors of HSV-2 infection included having two or more lifetime sexual partners for males and being Sikh (although marginal), ever being married or having had sex with a non-regular partner in the last year for females. While our analysis was adjusted for site, it is highly possible that religion is a confounder of site.

Our study has several limitations. Using the available DBS diagnostic technologies, it was only possible to measure lifetime exposure rather than current infections. Owing to the sample size, it was not possible to determine the correlates of each STI within the different sites which could be different due to heterogeneity in behaviour patterns and historical trajectory of infections. Face-to-face interviews could lead to misreporting due to social desirability bias. In fact, of females reporting never having had sex, 2.4% and 1.2% were positive for HSV-2 and syphilis, respectively. Sampling was not random, as we selected SRS sites that were conveniently located close to the study coordinating centres. Finally, we were able to explore the impact of people who were missed in the survey on study outcomes as the demographic variables between those who migrated out, were present but refused to participate and participated (online supplementary tables 1, 4) could be compared using the SRS sample frame. We found some

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Table 3 Final multivariable model for Herpes Simplex Virus-2

Level	Type of variable	Characteristic	Males OR* (95% CI)	Females OR* (95% CI)
Level 1 (distal variables)	Socio-demographic	Age	1.04 (1.0 to 1.1)	1.02 (1.0 to 1.0)
		Site†		
		Bangalore	0.7 (0.5 to 1.0)	0.7 (0.5 to 0.9)
		Hyderabad	2.1 (1.5 to 3.0)	1.9 (1.4 to 2.7)
		Chandigarth	0.7 (0.5 to 1.1)	0.8 (0.5 to 1.1)
		Religion		
		Hindu	1.0	1.0
		Christian	4.4 (2.1 to 9.0)	2.8 (1.4 to 5.7)
		Sikh	2.2 (1.0 to 4.8)	2.2 (1.1 to 4.5)
		Muslim	1.1 (0.1 to 9.0)	1.1 (0.2 to 5.5)
		Marital status		
		Never married		1.0
		Ever married		4.1 (1.2 to 13.7)
		Education		
		Graduate	1.0	1.0
		Primary	0.8 (0.4 to 1.4)	1.4 (0.8 to 2.8)
		Illiterate	1.0 (0.5 to 1.9)	1.5 (0.8 to 2.6)
Level 2a (proximal variables)	Non-sexual behaviour	Syphilis status		
		Negative	1.0	1.0
		Positive	6.2 (2.2 to 17.4)	5.6 (1.7 to 17.8)
		Alcohol consumption		
		None	1.0	1.0
		1–2 times per week	0.5 (0.2 to 1.0)	1.3 (0.7 to 2.5)
		≥3 times per week	1.0 (0.5 to 1.9)	0.6 (0.2 to 1.7)
		Ever smoking		
		No	1.0	
		Yes	1.1 (0.6 to 1.9)	
Level 2b (proximal variables)	Sexual behaviour	Lifetime no of partners		
		1	1.0	
		≥2	2.8 (1.1 to 7.4)	
		Non-regular partner in last year		
		No	1.0	1.0
		Yes	0.3 (0.0 to 1.6)	4.7 (1.2 to 18.7)

The multivariable logistic regression model was constructed using backward elimination. At each level, we show only the variables that remained in the final model.
*ORs are calculated by adjusting each variable to city, site and the variables that remained in the model from the previous and same levels.
†The referent group is the entire sex- and site-specific study population.

demographic variables to differ between those who were missed from the survey and those who participated.

Our study reveals some important insights on general population surveys to study STIs. Collection of blood through DBS resulted in very low refusal rates (4.4%). It is possible to measure lifetime exposure to HSV-2 and syphilis infections using DBS, which makes population-based surveys cost-saving and feasible. Self-reporting of sexual behaviour could provide some picture of sexual activity but may not, by itself, be sufficient to fully capture the spectrum of sexual activity within the population. It is important to complement such face-to-face surveys with other non-biased methods such as polling booth surveys or in combination biological parameters, especially among women.

While this and other studies provide critical insights into STIs in India, there is an urgent need for a national STI surveillance

Key messages

- The prevalence of HSV-2 is geographically heterogeneous (ranging from 5.8% to 17.8% within the surveyed geographies), while that of syphilis is not (average of 1.7%).
- Predictors of HSV-2 and syphilis vary and include geographic, demographic and behavioural variables.
- STI surveillance based on biological parameters is preferable to self-reported sexual behaviour, especially in females.
- Household sero-epidemiological surveys of STIs based on DBS at a national scale would be highly feasible and could help inform evidence-based programming.

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system that collects both behavioural and biological parameters to better estimate the true burden of STIs and understand the associated risk factors. Data emerging from the surveillance system would enable India to design and implement treatment centres based on need and help identify STI and HIV-prone geographies. A surveillance system based on DBS would be highly feasible and cost-saving.

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

Competing interests None.

Ethics approval Ethics approval was provided by 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).

Contributors SKS, PM and PJ were responsible for study design; SKS and PM provided oversight of study implementation; SKS wrote the manuscript and supervised all analyses; SJ managed the database; SJ and CM conducted the statistical analyses; RK and PB supervised the field studies in Chandigarh and Hyderabad, respectively; PM, PA, SJ, CM and PJ helped draft and review the manuscript; PJ was the PI for the study.

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