Original Contribution

Geographic Prevalence and Multilevel Determination of Community-level Factors Associated with Herpes Simplex Virus Type 2 Infection in Chennai, India

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Herpes simplex virus type 2 (HSV-2) is one of the most prevalent sexually transmitted infections, and it increases the risk of transmission of human immunodeficiency virus type 1 at least twofold. Individual-level factors are insufficient to explain geographic and population variation in HSV-2, suggesting the need to identify ecologic factors. The authors sought to determine the geographic prevalence and community-level factors associated with HSV-2 after controlling for individual-level factors among slums in Chennai, India. From March to June 2001, participants aged 18–40 years voluntarily completed a survey and were tested for HSV-2. Community characteristics were assessed through interviews with key informants and other secondary data sources. Multilevel non-linear analysis was conducted. Eighty-five percent of eligible persons completed the survey; of these, 98% underwent HSV-2 testing, producing a final sample of 1,275. Participants were of Tamil ethnicity, were predominantly female and married, and were on average 30 years old. Fifteen percent were infected with HSV-2, and there was significant variation in HSV-2 prevalence among communities. After controlling for individual-level factors, the authors identified community-level factors, including socioeconomic status and the presence of injection drug users, that were independently associated with HSV-2 and explained 11% of the variance in prevalence. Future studies are needed to test mechanisms through which these community-level factors may be operating.

disease transmission; herpesvirus 2, human; residence characteristics; risk factors; sexually transmitted diseases, viral; simplexvirus

Abbreviations: HIV-1, human immunodeficiency virus type 1; HSV-2, herpes simplex virus type 2; SD, standard deviation; SES, socioeconomic status; STI, sexually transmitted infection.
with sexually acquired HIV-1 have active HSV-2 infection (10).

HSV-2 seroprevalence studies show variation in infection by geographic location. Some of the highest prevalences of HSV-2 have been found in Africa and the Americas. Lower prevalences have been found in Western and Southern Europe than in Northern Europe and North America, and although there have been few studies, the lowest prevalence has been seen in Asia (2, 9, 11–15). There also is a great deal of variation within regions. In India, HSV-2 prevalences of over 40 percent have been reported in STI clinics in Pune (8), but in a study of low-risk blood donors in Vellore, 15 percent of females and 10 percent of males were infected (16). HSV-2 prevalence has also been found to vary by individual-level characteristics, including gender, age, sexual activity level, marital status, socioeconomic status (SES), education, and race/ethnicity (9, 11, 13). However, these characteristics are insufficient to explain differences within and between countries, regions, and population subgroups, suggesting the need to identify ecologic factors which may help to explain the differences (11, 17).

To determine whether and to what extent ecologic factors are causal determinants of differences in HSV-2 risk, a multilevel approach is required wherein individual and ecologic factors are simultaneously added to a model (18). This approach has gained popularity as the importance of multiple sources of STI transmission risk has become increasingly apparent (19). The growth in statistical and computational tools needed to study multilevel models gives evidence of their growing popularity and has advanced approaches to investigation. A stronger influence, however, on expanding models of STI risk (and other public health issues) to include ecologic factors is the mounting evidence that ecologic factors may help explain disparities in diseases such as HSV-2, yielding new avenues for disease prevention and control. A first step in the determination of causal ecologic factors is to develop hypotheses about community-level factors which may be associated with HSV-2 and ultimately HIV-1. Developing such hypotheses requires an understanding of the study setting.

The current study was conducted in Chennai, the capital of Tamil Nadu State in southern India. Chennai is a city of 6 million people containing extensive slums. In Chennai and similar cities in India, the highest rates of STI and HIV-1 infection have been found among sex workers, men who have sex with men, and injection drug users (20, 21), attributable in part to migratory work and related sex-work patterns (22). It is estimated that approximately 85 percent of HIV-1 transmission occurs through sexual contact, although injection drug use is an important risk factor in northeastern India (20). STI and HIV-1 transmission patterns are also related to diverse cultural, social, religious, and sexual practices in India (22).

Building on this evidence, we developed exploratory hypotheses that community-level factors, such as the presence of brothels, working men’s quarters, men who have sex with men, and substance abuse, may serve to increase the likelihood of sexual partnering with an HSV-2-infected person, resulting in increased risk of individual HSV-2 infection (figure 1). We explored these hypotheses by collecting individual and community information in selected slums in Chennai. Our objectives in this study were to determine the geographic prevalence of HSV-2 infection and to determine community-level factors associated with HSV-2 infection after controlling for individual-level factors.

**MATERIALS AND METHODS**

**Overview**

The study was conducted from March to June of 2001 in Chennai. The methods of the study have been presented previously (23). Briefly, 965 urban residential communities were designated by the Tamil Nadu Slum Clearance Board as “slum communities.” On the basis of power and sample size calculations conducted for the parent study, a community cluster randomized trial, we determined that 24 communities would be required from each site (Chennai, China, Peru, Russia, and Zimbabwe). We selected 30 communities in Chennai to ensure that sufficient candidate communities were available for the parent study. The communities were selected according to a number of characteristics to permit comparability among the communities, to improve our ability to measure intervention efficacy, and to maximize the cost-efficiency of the parent study. All selected communities had 100–300 residents, were named, were distinct neighborhoods, were geographically isolated from one another, and had single-story structures.

Trained field-workers enumerated households, and 65 households containing at least one person aged 18–40 years were selected by systematic random sampling. Among households with more than one eligible individual, only one person was selected for participation by simple random sampling (24). Field-workers invited the selected person to participate in the study, and the individual and his or her family were invited to attend a community health camp. There was no more than a month between household enumeration and attendance at the health camp. The study methods, procedures, and informed consent forms were approved by institutional review boards at the Johns Hopkins Bloomberg School of Public Health and the Y. R. Gaitonde Centre for AIDS Research and Education. Informed consent was obtained before collection of all data.
Procedures

At the community health camps, participants answered a survey using computer-assisted personal interviewing and were given a physical examination that included testing for HSV-2. The surveys were conducted in private areas in the Tamil language by same-sex, trained interviewers. The survey included items on sociodemographic factors, sexual behavior, history of STIs, drug use, and other topics. HSV-2 testing was conducted in the Chennai study laboratory by means of the HerpeSelect 2 enzyme immunoassay (Focus Diagnostics, Inc., Cypress, California). A registered nurse conducted the blood draw for HSV-2 antibody testing in a setting conducive to infection control procedures. Twenty percent of all biologic specimens were sent to Johns Hopkins University School of Medicine (Baltimore, Maryland) for quality control. All services were free, and no monetary incentive was offered for participation.

A second survey was conducted among key informants to assess community characteristics such as SES and evidence of community-level STI risk factors (25). Staff of the Y. R. Gaitonde Centre for AIDS Research and Education, who were familiar with the study areas, were trained in ethnographic field methods. Briefly, staff identified approximately 10 key informants— influential representatives and other persons knowledgeable about the community. Verbal informed consent was elicited from the key informants; no one refused participation. Key informants were asked questions on a standardized list of community-level measures.

Data on two additional community-level measures were also obtained. Staff counted the number of wine shops in each community, and they obtained from the slum clearance board the number of years each slum had been in existence.

Measures

Level 1: individual-level measures. Trained interviewers asked participants about the following selected sociodemographic factors: ethnicity, age, sex, marital status, participation in migratory work during most years, circumcision status (males only), and educational level. Participants were also asked about the following selected STI risk behaviors: STI history, number of casual sex partners in the past 3 months, and drug abuse (“In the past 3 months, have you used drugs, e.g., marijuana, cocaine, heroin, amphetamines, barbiturates, inhaled glue or solvents, or any other drug to get high?”).

Level 2: community-level measures. Information on community-level measures, including measures of SES and STI risk factors, was collected in each community.

Socioeconomic status. Key informants were asked five SES-related questions regarding electricity structures, water structures, housing and roofing materials, and number of persons per household. For the creation of summary measures by community, the first four items were summarized separately as the proportion of key informants agreeing on the presence of electricity and water structures and on whether building and roofing materials were thatch or non-thatch. Numbers of people per household were averaged across the key informant responses.

We conducted a principal-components analysis of the five items plus years of existence of the community to identify one community-level measure of SES. One factor with an eigenvalue of 2.78 emerged from four out of six of the community-level SES items, including electricity and water structures and housing and roofing materials. The factor showed good reliability, with a Cronbach’s alpha of 0.85. From those four items, using regression methods, we created one scale with a mean of 0 and a variance equal to the squared multiple correlation between the estimated factor scores and the true factor values. The remaining two SES measures—average number of people per household and years of existence of the slum—were analyzed as separate measures.

Community-level STI risk factors. We assessed six community-level STI risk factors. Five were based on key informant reports and the sixth was based on field staff observations. Key informants in each community were asked to report on the existence of working men’s quarters, brothels, men who had sex with men, injection drug users, and public intoxication. Key informants’ responses were coded as present or absent. For each slum, a summary measure for each risk factor was created on the basis of the percentage of key informants from each slum reporting the presence of each risk factor (the implicit assumption being that the higher the percentage of key informants endorsing the presence of a risk factor, the more likely the factor was to actually be present in the slum). The sixth item was the number of wine shops in the community; wine shops were counted by staff, and the raw count was used.

Statistical analysis

The data in the study formed a nested structure; that is, the participants (level 1) were nested within the communities (level 2). Because of this data structure, multilevel models represented the most appropriate method of analysis. Multilevel analysis accounts for nonindependence of observations within groups, uses empirical Bayes adjustments for the group means, and allows for significance testing of the between- and within-group (levels) variances on the outcome, HSV-2.

Exploratory analysis was conducted and summary statistics were generated for the individual-level (level 1) variables and the community-level (level 2) variables using Stata Intercooled, version 8.0 (Stata Corporation, College Station, Texas), and HLM, version 6.02 (Scientific Software International, Inc., Lincolnwood, Illinois). Maps of HSV-2 prevalence by community were created using MapInfo, version 7.0 (MapInfo Corporation, Troy, New York). A series of models was generated to determine whether and to what extent community-level factors significantly explained HSV-2 prevalence after controlling for individual-level factors in multilevel nonlinear modeling. First, random-effects analysis of variance was conducted to assess the extent of variation in HSV-2 prevalence between the communities and to test the significance of the variation. Next, an
exploratory ecologic analysis was conducted to determine the association of the community-level variables to HSV-2 prevalence. Then analysis of covariance was conducted to determine which of the level 1 variables were significantly associated (two requirements—the 95 percent confidence interval did not include 1 and the \( p \) value was less than 0.05) with individual-level HSV-2. Finally, a means-as-outcomes regression model was developed which began with the significantly associated level 1 factors and then added in all level 2 factors. Level 2 variables which were the least significant were subtracted one by one from the model until a final model which contained only variables that were significant at levels 1 and 2 remained.

By generating Akaike and Bayesian information criteria values, we assessed the goodness of fit and parsimony of the model. Akaike’s information criterion considers the number of model parameters, and the Bayesian information criterion considers the effect of model parameters and sample size (26, 27). To date, HLM software does not produce values for Akaike’s information criterion or the Bayesian information criterion; we used Stata for these calculations. Actual fit was assessed by residual analysis. At the community level, we created a Q-Q plot of the Mahalanobis distance—that is, the standardized squared distance of a unit from the center of a \( v \)-dimensional distribution, where \( v \) is the number of random effects per unit used to diagnose fit, versus the expected values of the order statistics for a sample of size \( J \) from a population that is distributed \( \chi^2(v) \).

### RESULTS

**Study population**

Of an estimated 14,000 adults living in the 30 communities, 1,947 (13 percent; 969 men and 978 women) were selected to participate in the study. Among selected individuals, 1,656 (85 percent) completed the survey, and of these, 1,631 (98 percent) provided samples for STI testing. Persons less likely to complete the survey were more often male (34 percent male vs. 54 percent female; \( \chi^2 p < 0.01 \), more often married (77 percent married vs. 71 percent unmarried; \( \chi^2 p < 0.01 \)), and slightly older (mean age ¼ 29.4 years vs. 28.5 years). Those who completed the survey but did not provide a biologic sample (vs. those that did) were more likely to be female, married, and slightly older, although they did not differ from the study population in terms of education, health status, or lifetime number of partners (data not included). Additionally, 309 participants (19 percent) reported no lifetime sexual activity and were excluded because they were not at risk for HSV-2.

At level 2, data were collected from 29 communities, and the average number of key informants was 10 (standard deviation (SD), 0.57; range, 9–11). Upon inspection of the data, 47 participants (4 percent) were excluded from further analysis because one slum had only one respondent and another slum did not have any data because it was dissolved before data collection. Thus, the final study sample included...
1,275 participants from 28 communities with an average of 46 participants per community.

**Characteristics of the study population**

Individual-level demographic and behavioral characteristics are shown in Table 1, summarized and stratified by HSV-2 status. In terms of individual-level characteristics, 100 percent of participants were of the Tamil ethnic group, and women constituted 57 percent of the population. Fifteen percent of the population was infected with HSV-2. The average age of the study participants was 30 years; 86 percent of participants were married, and 28 percent had a college degree. Twenty-six percent of participants participated in migratory work during most years, and 10 percent of males were circumcised. Four percent reported having had at least one casual sex partner in the past year, with an overall reported average of 0.20 casual partners in the past year. Seven percent of participants had used a drug to get high in the past 3 months, and 6 percent had a history of an STI.

Community-level characteristics were summarized across communities. In terms of SES, electricity and water structures existed in 86 percent and 43 percent of communities, respectively. Thatch material was used in home and roof construction in 61 percent and 57 percent of communities, respectively. The average number of persons per household was 5.25 (SD, 0.67), and the mean of the variances within each community was 0.30 (SD, 0.51). The average number of years a slum had been in existence was 28.71 (SD, 14.42; range, 1–60). Table 2 provides the percentage of key informants reporting on the existence of five community-level STI risk factors averaged across the slum communities. On average, 3 percent of key informants reported their slums as having working men’s quarters, 14 percent reported brothels, 28 percent reported men who had sex with men, 47 percent reported injection drug users, and 43 percent reported very often or frequent public intoxication. On average, 3.25 (SD, 2.94; range, 1–12) wine shops were counted per community.

**Analysis-of-variance model**

Figure 2 shows a map of Chennai with the HSV-2 prevalence for each community. The mean HSV-2 prevalence was 15.37 (SD, 36; range, 4.17–49.06). The multilevel analysis-of-variance model showed a significant amount of variation (30 percent; \( \chi^2, p < 0.00 \)) in HSV-2 prevalence between the communities. Given these findings, we proceeded to the ecologic model.

**Ecologic model**

To determine which community-level factors were associated with HSV-2 prevalence, we generated an ecologic model (Table 3). Since this model was intended to be...
TABLE 3. Individual- and community-level characteristics associated with individual-level herpes simplex virus type 2 infection in selected slum communities, Chennai, India, 2001†

<table>
<thead>
<tr>
<th>Individual-level characteristics</th>
<th>Ecologic OR†</th>
<th>95% CI‡</th>
<th>Analysis of covariance OR</th>
<th>95% CI</th>
<th>MAOR†</th>
<th>95% CI</th>
<th>Final model adjusted OR</th>
<th>95% CI</th>
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<td>Intercept</td>
<td>0.15**</td>
<td>0.06, 0.37</td>
<td>0.01**</td>
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<td>0.01**</td>
<td>0.00, 0.02</td>
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<td>Age (years)</td>
<td>1.05**</td>
<td>1.03, 1.07</td>
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<td>1.07, 1.14</td>
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<td>1.07, 1.13</td>
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<td>Male</td>
<td>0.79*</td>
<td>0.66, 0.95</td>
<td>0.48**</td>
<td>0.32, 0.71</td>
<td>0.48**</td>
<td>0.32, 0.72</td>
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<td>Marital status</td>
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<td>Married</td>
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<td>Widowed/separated/divorced</td>
<td>1.55**</td>
<td>1.15, 2.08</td>
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<td>Single/never married</td>
<td>0.73</td>
<td>0.50, 1.08</td>
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<td>College degree or more</td>
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<td>High school diploma</td>
<td>1.05</td>
<td>0.85, 1.30</td>
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<td>Primary school or less</td>
<td>1.32**</td>
<td>1.10, 1.58</td>
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<td>Engaging in migratory work during most years (n = 598)</td>
<td>1.11</td>
<td>0.69, 1.80</td>
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<td>Circumcised (males only) (n = 535)</td>
<td>1.12</td>
<td>0.47, 2.68</td>
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<td>No. of casual sex partners in the past year</td>
<td>1.03*</td>
<td>1.01, 1.05</td>
<td>1.04*</td>
<td>1.00, 1.08</td>
<td>1.04*</td>
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<td>Ever having a sexually transmitted infection</td>
<td>1.31</td>
<td>0.88, 1.96</td>
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<td>Using drugs to get high in the past 3 months</td>
<td>1.44*</td>
<td>1.02, 2.03</td>
<td>2.33*</td>
<td>1.16, 4.67</td>
<td>2.35*</td>
<td>1.17, 4.72</td>
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<td>Community-level characteristics, as reported by key informants (n = 28)</td>
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<td>Socioeconomic status</td>
<td>0.70*</td>
<td>0.55, 0.90</td>
<td>0.81*</td>
<td>0.70, 0.95</td>
<td>0.75*</td>
<td>0.59, 0.96</td>
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<td>Average no. of persons per household</td>
<td>1.03</td>
<td>0.73, 1.46</td>
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<td>1.00</td>
<td>0.70, 1.43</td>
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<td>Average no. of years of slum’s existence</td>
<td>1.01*</td>
<td>1.00, 1.02</td>
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<td>1.01*</td>
<td>1.00, 1.02</td>
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<td>% of key informants reporting:</td>
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<tr>
<td>Working men’s quarters</td>
<td>1.35</td>
<td>0.82, 2.23</td>
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<td>0.72</td>
<td>0.26, 2.0</td>
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<td>Brothels</td>
<td>1.12</td>
<td>0.76, 1.66</td>
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<td>1.68</td>
<td>0.86, 3.27</td>
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<td>Men who had sex with men</td>
<td>0.57</td>
<td>0.31, 1.01</td>
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<td>0.48*</td>
<td>0.24, 0.97</td>
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<tr>
<td>Injection drug users</td>
<td>1.76*</td>
<td>1.03, 3.03</td>
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<td>1.70</td>
<td>0.99, 2.93</td>
<td>1.95*</td>
<td>1.15, 3.30</td>
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<td>Public intoxication (very often and frequently)</td>
<td>1.63</td>
<td>0.94, 2.83</td>
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<td>0.99</td>
<td>0.97, 1.02</td>
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<tr>
<td>Average no. of wine shops</td>
<td>0.96</td>
<td>0.92, 1.00</td>
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<td>1.64</td>
<td>0.94, 2.89</td>
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<td>Tau</td>
<td>0.18</td>
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* p < 0.05; **p < 0.01.
† All models represent multilevel nonlinear models.
‡ OR, odds ratio; CI, confidence interval; MAOR, means as outcomes regression.

exploratory, we entered all community-level factors into the model, including SES, number of persons per household, years of slum existence, working men’s quarters, presence of brothels, presence of men who had sex with men, presence of injection drug users, frequency of public intoxication, and number of wine shops. SES and the presence of injection drug users had 95 percent confidence intervals that did not include 1 and p values that were less than 0.05.

**Analysis-of-covariance model**

To determine which individual-level factors were associated with individual-level HSV-2 infection after accounting...
for the clustering of participants within communities, we constructed a series of analysis-of-covariance models (table 3). Individual-level factors, including age, sex, marital status, education, migratory work, circumcision status (males only), number of casual sex partners in the past year, STI history, and drug use (use of drugs to get high in the past 3 months) were entered into the model. Increased age, male sex, higher numbers of casual sex partners, and likelihood of drug use were all significantly related to individual-level infection with HSV-2 and were retained at level 1.

Final model

Next, to determine the extent to which community-level variables were associated with HSV-2 infection, we constructed a series of means-as-outcomes-regression models (table 3). In the first model, we included all community-level factors. Insignificant factors were subtracted, resulting in a final model with factors (SES and the presence of injection drug users) that had 95 percent confidence intervals which did not include 1 and \( p \) values less than 0.05. In the final model controlling for individual-level factors, a one-unit increase in community-level SES was associated with an odds ratio of 0.75 (95 percent confidence interval: 0.59, 0.96), which indicates a reduction of 25 percent in the odds of HSV-2 infection in the community. A one-unit increase in the proportion of injection drug users in the community, on the other hand, was associated with an odds ratio of 1.95 (95 percent confidence interval: 1.15, 3.30), which indicates an increase of 95 percent in the odds of HSV-2 infection in the community. In the final model, the significant level 2 factors helped to explain an additional 11 percent of the variance associated with HSV-2 infection. Figure 3 further elucidates the results of the final model, showing HSV-2 prevalences by 30th percentile of SES and percentage of key informants reporting on the presence of injection drug users. Overall, the mean HSV-2 prevalence decreased with each 30th-percentile decrease in SES. Within low- and medium-SES slums, HSV-2 prevalence increased for each 30th-percentile increase in percentage of injection drug use. In high-SES slums, HSV-2 prevalence remained the same or decreased slightly (not statistically significant) for each 30th-percentile increase in percentage of injection drug use.

The Akaike and Bayesian information criterion values for the model with only level 1 factors were 1,013.59 and −45.72, respectively. The Akaike and Bayesian information criterion values for the final model with significant level 1 and level 2 factors were 987.05 and −61.97, respectively. The lower values for the final model with significant level 1 and level 2 factors suggest a better fit and greater parsimony than was seen for the model with level 1 factors alone. The Q-Q plot also suggests a good-fit model with no serious departures from normality.

DISCUSSION

Among these communities, we identified considerable differences in the prevalences of HSV-2 infection, which ranged from 4.17 percent to 49.06 percent. These findings are similar to those of a large number of studies that have found geographic heterogeneity in HSV-2 and other STIs (2, 9, 11–15). After controlling for significant individual factors for HSV-2, including age, sex, number of casual sex partners in the past year, and drug use, we identified community-level factors (including SES and the presence of injection drug users) which were independently associated with HSV-2 prevalence and which explained 11 percent of the variance.

The current study was not designed to test the mechanisms through which potential STI risk factors at the community level may increase individual-level risks of HSV-2 infection, yet it represents the first step in the determination of community-level factors and their independent associations with HSV-2. The potential importance of community-level risk factors for HSV-2 and other STIs begins with the recognition that sexual partnerships are often formed in tightly confined social settings that have spatial and cultural boundaries (28, 29). These settings become, in a sense, sexual marketplaces, since they provide the types of individuals and opportunities available for partnering, as well as the social rules that guide the selection of sex partners (28). Research in India and other Asian countries suggests that STI and HIV-1 transmission patterns are partly related to sexual marketplaces and their players, such as commercial sex workers and men who have sex with men (20, 30–32). For example, sex work in Chennai is not structurally organized as is the case in other cities in India, such as Mumbai or Calcutta. Rather than a "red light district" with large brothels, sex work in Chennai is based on small groups of women either working the streets under the protection of a pimp or working "freelance" (as in the case of housewives). While men may seek sex partners at some distance from their homes to avoid unwarranted recognition, the majority of the men included in the survey reported selecting sex partners near their place of residence.

A number of studies have also found structural-level community factors such as SES to be associated with STI.
prevalence, and other studies have found the same with drug users. One hypothesis is that impoverished slums may have more drug users, and concentration of drug users within a community may alter sexual marketplaces by altering sex partner selection patterns and sex network structures. Drug markets, like sex marketplaces, have been described as having dense networks with specific mixing patterns and local geographic characteristics (33), and they overlap with the networks of commercial sex workers and men who have sex with men (34–37), providing the potential for transmission and acquisition of STIs within and between these networks.

There is good evidence suggesting connections between high-risk groups and lower-risk groups within communities. For example, in Chennai, approximately one quarter of HIV-1-infected patients are housewives who are otherwise at low risk (20). Our finding of an association between individual-level HSV-2 infection and the presence of injection drug users at the community level suggests that drug networks may increase the likelihood of selecting a sex partner who is infected with an STI and may play an important role in transmission of STIs and HIV-1 to lower-risk community members.

The current study had a number of limitations. The selection of communities was restricted to allow for comparability in the parent trial, possibly resulting in a biased sample of communities. We were unable to assess this possible bias, as there are no statistics maintained by the slum clearance board on the slums. Thus, results may only be generalizable to slum communities with a similar profile. Women were slightly more likely to participate in this study than males, since they are more likely to be in residence in the slums. In addition, the current study was not designed to directly test causality or the mechanisms through which potential STI risk factors at the community level may increase individual-level risks for HSV-2. Future studies should be designed to carefully measure drug use at the individual and community levels to determine whether the independent effects identified in this study are valid or in fact result from misspecification of the community-level variables.

Despite these limitations, this study obtained data which provide a stepping-stone for future studies attempting to identify community- or structural-level determinants of HSV-2 disparities among population subgroups and communities. The identification of these structural determinants may yield important prevention and intervention opportunities for limiting HSV-2 and HIV-1 transmission.

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REFERENCES

32. Lau JT, Wong WS. HIV antibody testing among male commercial sex networkers, men who have sex with men and the lower-risk male general population in Hong Kong. AIDS Care 2002;14:55–61.