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Demographic and behavioral characteristics of male sexually transmitted disease patients in Japan: a nationwide case-control study.

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Short summary: The nationwide case-control study in Japan found that male STD patients are highly educated, and that STI risks exist universally across various types of sexual practices and sexual partnerships.

ABSTRACT

Backgrounds: Sexually transmitted infections (STIs) increased rapidly in Japan during the 1990s. **Methods**: To determine the epidemiological characteristics of STI patients, male cases (n=765) from 21 clinics across Japan and controls from the general population (n=1167), both aged 18-59 years, were compared using two data sets of nationwide sexual behavior surveys conducted in 1999. **Results**: Male STI patients were more likely to be under 40 years of age (OR=3.94, 95% CI: 2.17, 7.15), unmarried (OR=2.65, 95%CI: 1.80, 3.91), and at least college/university educated (OR=2.03, 95% CI: 1.45, 2.83). They were also more likely to have had multiple partnerships in the previous year (OR=3.33, 95% CI: 2.20, 5.05 for 2-3 partners, OR=6.29, 95% CI: 3.81, 10.37 for ≥4 partners), unprotected vaginal sex with regular partners (OR=2.70, 95% CI: 1.75, 4.17), unprotected vaginal and/or oral sex with casual partners (OR=2.14, 95% CI: 1.40, 3.26), and unprotected vaginal (OR=2.64, 95% CI: 1.46, 4.80) and oral sex with paid partners (OR=4.72, 95% CI: 3.04, 7.32) in the previous year. **Conclusions:** These results suggest that male STI patients in Japan are highly educated and have a diverse occupational background, and that STI risks exist universally for various types of sex and sexual partnerships.

Keywords : Keywords: case-control study, clinics, patients, male, sexually transmitted infection.

INTRODUCTION

According to the sexually transmitted infection (STI) surveillance in Japan, STIs, especially non-viral STIs, began to increase rapidly in the mid 1990s. The increase between 1995 and 1998 was over 30 percent for chlamydial and gonococcal infections in both genders (1-2). Although surveillance information was interrupted due to a nationwide reorganization of sentinel sites in 1999, an increase in these STIs continued thereafter, reaching a peak in 2002 (3). Currently, patients less than 30 years old account for 47% and 68% of all male and female cases, respectively, and genital chlamydia and gonorrhea are the most dominant STIs among both genders. STI surveillance provides useful information regarding trends in STIs. However, since demographic variables in the surveillance are limited only to age, gender and residential area, questions remain about what types of sexual behaviors in what subpopulations contributed to the recent increase in STIs in Japan. Such information is vital for developing effective STI/HIV prevention efforts (4-5). The present study was conducted to obtain insight into this research question.

MATERIALS AND METHODS

Study design

This was a case-control study in which cases and controls were selected from two data sets of sexual behavior surveys conducted in 1999 in Japan, one from a sample of STI patients and the other from a probability sample of the general population. We were able to

combine these data sets since both were designed by the same authors (MOK, MK, TH) who used the same set of survey questions, other than those specific to each study.

Sexual behavior survey of the general population (6). This survey was conducted during June-July of 1999. A sample of 5000 individuals, aged 18-59 years, was selected from the general population using a 2-stage random sampling procedure. Briefly, the entire country was divided into 11 regions. Each region was further divided into 5 population density bands, yielding 57 strata. A total of 5000 samples were then allocated for each stratum proportionally to the population size. Within each stratum, sampling wards from which 9-22 samples were drawn systematically from residents' basic register or electoral register were selected randomly using the list of wards prepared for the census survey. Each subject was visited by a trained staff 4 times at most when absent and asked to complete an anonymous self-administered questionnaire. A total of 3562 subjects (1762 males, 1800 females) were sampled without replacement, yielding a final response rate of 71.2 percent.

Nationwide STI patient survey. This survey was conducted during July-September of 1999. STI patients were recruited from 21 private STI clinics in 7 large cities (Sapporo, Sendai, Tokyo, Osaka, Hiroshima, and Fukuoka) within 6 districts (Hokkaido, Tohoku, Kanto, Kansai, Chugoku, and Kyushu) of Japan. These clinics were recruited through consultation with local STI physicians' associations and chosen based on their proximity to the largest entertainment district of each city. Subjects were selected from patients who visited the clinic during the

study period if they were diagnosed with STIs or typical STI symptoms. STIs included chlamydial infection, gonorrhea, syphilis, non-chlamydial non-gonococcal urethritis, genital herpes, condyloma acuminatum, chancroid, phthirus pubis, and typical STI syndrome included unusual genital discharge (flow), sores, warts, burning with urination, and redness or itching around the penis. Eligible participants were consecutively recruited and asked to complete an anonymous self-administered questionnaire in a waiting room. A total of 1119 subjects participated in the survey, yielding a final response rate of 84.9 percent (791 males, 304 females, 24 unknown gender). Because the survey was anonymous, not all patients responded and information from the clinic could not be linked to the survey, the distribution of the types of STIs or typical STI symptoms among participants was not determined.

Integration of the data sets

The data sets of the two surveys were combined for male subjects aged 18-59 years who lived within the 6 districts previously described and who had sexual intercourse during the previous year. The merged data set included information about age, gender, occupation, educational background, marital status, HIV/STI-related knowledge (17 items), age at first sex, number of sexual partners in the previous year, types of sexual partners (regular, casual, or paid) in the previous year, types of sex (vaginal, oral, or anal), and condom use with each type of sexual partner in the previous year or at the last sex. Female subjects were also excluded to avoid potential bias, given that 60 percent of them were recruited from a single

clinic.

Sample characteristics

Compared to the 2000 census data (7), the control group was slightly older. The proportion of subjects in their 20s, 30s, 40s and 50s was 17, 23, 29 and 30 percent, respectively, for controls and 26, 24, 24 and 27 percent, respectively, for the male census population. Controls were less unmarried than census population (20 percent vs. 39 percent) and were slightly more educated (45 percent vs. 34 percent for at least a college/university education). Occupational pattern was similar between the populations. Regarding STI cases, only age was available for comparison with the 1999 national sentinel STI surveillance data (8). STI cases in this study were slightly older than the STI surveillance population where the proportion of subjects in their 20s, 30s, 40s and 50s was 44, 37, 14 and 5 percent, respectively, for cases, while they were 51, 31, 13 and 5 percent, respectively, for the STI surveillance population.

Ethical issues

In both surveys, verbal informed consent was obtained from the participants. Then they were asked to fill out the questionnaire and return it in a sealed envelope, in person or by mail. This research study was approved by the Committee for Research on Human Subjects at Kyoto University in Japan.

Statistical analysis

All statistical analyses were performed using SPSS for Windows (version 12.01; SPSS Inc., Chicago, Illinois, USA). Bivariate analyses were performed to determine the association between STI infection and demographic and behavioral variables. Logistic regression was performed to calculate adjusted odds ratios (AOR) and 95 percent confidence intervals (CI). Answers to HIV/STI knowledge questions were transformed into scores by giving 1 for a correct answer and 0 for an incorrect answer. Behavioral variables were combined to create variables that coded the presence (=1) or absence (=0) of unprotected sex for each type of sex with each type of partner. These variables were compulsorily entered into a multivariate model, together with age at first sex, number of sexual partners in the previous year, and demographic variables except for the variables of behaviors practiced by too few participants and those strongly interrelated. All statistical tests were two-tailed and results were considered significant when $p<0.05$.

RESULTS

There were 765 cases and 1167 controls. Those who had STI in the previous year (n=16) were excluded from the control group.

Table 1 compares the demographic characteristics and HIV/STI-related knowledge of the groups. STI patients were much younger than the controls (average age 31.8 years vs. 41.6 years, $p<0.001$). There were less self-employed and more unemployed individuals among the cases compared to the controls. Although statistically significant ($p<0.001$),

occupational differences between the groups were small. There was a significant difference in marital status. While 20 percent of the controls were unmarried, it was 66 percent among STI patients ($p<0.001$). STI patients were significantly more educated than the controls, with 65 percent of cases having at least a college/university education compared to 45 percent of the controls ($p<0.001$). Average scores on HIV/STI-related knowledge were both significantly greater in STI patients than in the controls ($p<0.001$).

STI patients experienced first sex approximately 2 years earlier than the controls and there was a large difference in the number of sexual partners in the previous year (Table 2). Compared to only 6.1 percent of the controls, 53 percent of STI patients reported having at least 4 sexual partners. More than 50 percent of STI patients reported having casual or paid partners in the previous year, compared to only around 10 percent among the controls. Regarding the prevalence of unprotected sex, the largest differences between the groups were observed in vaginal and oral sex with casual or paid partners. It was 26-49 percent among STI patients, but only 6.3 percent, at most, among the controls. There were slightly but significantly more STI patients who experienced unprotected oral sex with regular partners in the previous year than the controls. Although unprotected anal intercourse with casual or paid partners was also significantly more common among STI patients than the controls, it was only around 2 percent even among STI patients. Proportion of men who had sex with men was 3.2 % among STI patients in the previous year, while it was 1.2% among general

population in lifetime.

Multivariate analysis was performed to evaluate the independent association of demographic and behavioral variables with STI infection (Table 3). Age, occupation, number of sexual partners in the previous year, and district variables were entered collectively into the model, together with other demographic and behavioral variables that were entered as dichotomous variables. HIV/STI-related knowledge scores were excluded from the analysis. Unprotected anal sex, which was too few, was also excluded from the analysis as well as the sex between men since time frame for question was different between the studies. Variables representing unprotected oral sex and vaginal sex with casual partners were combined to create a single dichotomous variable that represents the presence or absence of unprotected oral and/or vaginal sex, since these variables were closely correlated ($r=0.802$).

Results of the multivariate analysis showed that STI patients were more likely to be under 40 year-old, unmarried, have at least a college/university education, while occupational categories showed little association. STI patients were more likely to have multiple partners, unprotected vaginal sex with regular partners, unprotected oral and/or vaginal sex with casual partners, and unprotected oral and vaginal sex with paid partners.

As indicated in Table 3, magnitude of association for some variables was greatly reduced in the multivariate analysis. Association showed largest recovery when both age and

marital status were removed from the model, suggesting that the results of the bivariate analyses were largely confounded by these variables. On the other hand, unprotected vaginal sex with regular partners, which was not significant in the bivariate analysis, became significant in the multivariate analysis. However, it became insignificant when all the demographic variables and the variable for the number of partners were removed from the model, suggesting that the effect of this variable was suppressed by a complex interaction of multiple variables.

DISCUSSION

As the first nationwide case-control study of STI infection using a probability sample for controls, this study characterized the demographic and behavioral profiles of Japanese STI patients in comparison to controls.

Compared to STI clinic-based case-control studies, case-control studies that used representative samples for cases and/or controls are limited in number. A British study used probability samples of the British National Surveys of Sexual Attitudes and Lifestyles (NATSAL) conducted in 1990 (n=13,765) (9) and 2000 (n=11,161) (10), in which cases were those who had STIs in the previous 5 years and controls were those who did not. In Slovenia, a national general population survey (n=1752) was conducted in 1999-2001 using the same design as the NATSAL, in which subjects who had STIs in their lifetime were compared to those who did not (11). In China, subjects with chlamydial infections diagnosed with urine

tests were compared to those uninfected among national probability samples (n=3426) in 1999-2000 (12). The National Health and Nutrition Examination Survey (NHANES) is a similar large-scale representative survey in the US using laboratory tests to determine STIs (13). It is less pertinent here, however, because published data to date has not included related analysis. Finally, case-control studies with cases and controls sampled from separate populations, as in this study, were conducted in the US and England. Gonorrhea cases (n=103) from the general Seattle population were compared to controls obtained through random digit dialing in 1995 (n=376) (14). In England, patients (n=20,516) from two STI clinics sampled during 1995-1996 were compared to the 1990 NATSAL population samples (15).

Multivariate analysis indicated that male STI patients were more likely to be under 40 year-old, unmarried, and have at least a college/university education, while occupation was not a significant predictor. Population-based case-control studies have consistently found that male STI patients are concentrated in younger age groups. Although the risk of STIs appeared to increase with age in the Slovenia study, it most likely reflected a lifetime history of STIs that was actually measured. The association of marital status and occupation with STI history was assessed in the NATSAL studies. As in this study, being unmarried was significantly associated with a greater STI risk among the 1990 NATSAL population, but not among the 2000 population.

Low socioeconomic status is a well established risk factor for STIs (16). Results of the China and Seattle studies support this association (12,14). However, such findings are not universal. Non-manual social class was found to be significantly more at risk for STIs among the 1990 NATSAL samples (9) and those with higher education were at increased STI risk in our study. Our findings may reflect the possibility that STI patients who actively sought medical care had higher education than those who did not. However, a recent cohort study showed that the general health practice index showed little association with educational background among urban middle-aged Japanese men (17).

The present study showed that STI patients were more likely to have multiple sexual partnerships, have unprotected vaginal sex with regular partners, unprotected vaginal and/or oral sex with casual partners, and unprotected vaginal or oral sex with paid partners.

Multiple sexual partnerships and sex with paid partners are well established risk factors (18) and consistently identified by population-based studies, except for the China and Seattle studies (12,14). In contrast, unprotected vaginal sex with regular partners was unexpected as a risk factor, since such an association was shown only in the China study (12). Two recent case series studies in Japan support this association. One study reported that STI patients were estimated to have been infected equally from regular, casual and paid partners (19), while another study reported that 48 percent of male gonococcal or non-gonococcal urethritis patients were estimated to have been infected from regular partners (20). It may be

that STI risk now exists even among regular partnership in Japan. Our finding was unlikely confounded with recurrent infections within regular partnerships, since similar findings were detected among new STI patients, as well as among those who experienced multiple STIs.

Although it has been well established that STIs, especially non-viral STIs, can cause orogenital infections (21-23), our study is the first population-based study that identified unprotected oral sex with paid partners as a risk factor for STI infection. This result is consistent with a recent clinical finding in Japan, where approximately half of the male gonorrhea patients appear to have been infected through oral sex with paid partners (19). This may be related to the fact that the oral sex industry has proliferated throughout the 1990s in Japan (24). Since oral sex and the use of paid sex are prevalent among youth (25), it is possible that oral sex plays an important role in STI transmission among young people. This concern is shared by a recent clinical finding that among STI patients, over 80 percent practiced oral sex, and approximately 50 percent practiced both oral and vaginal sex with multiple types of sexual partners (26).

Results of the present study should be interpreted with caution. Although the case-control design utilized here is pertinent for rare diseases such as STIs, the analytic value may be compromised compared with cross-sectional studies with a representative sample in which cases are nested. In the present study, STI cases were sampled from private clinics. This is because over 90% of medical institutions are private and because almost all people are

covered by medical insurance programs, which are equally applied to both private and public institutions in Japan. Important characteristics of the STI cases in the present study are shared with other studies. Among the 16 patients with STIs in the previous year who were excluded from the control population in the analysis, 9 (56.3%) reported to have paid for sex in the previous year. These patients are younger, more likely to be unmarried, and more educated than the general population sample. A high prevalence of paid sex was also observed in our nationwide sexual behavior survey among national university students in 1999 (n=13100). In that survey, 7 (43.8%) out of 16 male students who ever had a STI reported that they had paid for sex in the previous year (unpublished observation). A case series study from a public hospital in Japan also reported that 52% of 98 gonococcal or non-gonococcal urethritis male patients were identified to be infected through paid sex (19). Such a high prevalence of paid sex among STI patients may reflect the fact that more than 10% of males reported to have paid for sex in the previous year in our national general population survey, compared with less than 0.5% in the National Health and Social Life Survey in the US (27). Such a high proportion of paid sex among men (6-16%) has been also observed from the surveys or surveillances of general population in other Asian countries around 1999-2003 (28), suggesting that STD epidemiology in Japan may share more with other Asian countries than other industrialized nations. Among control subjects, although the response rate of our survey (71.2%) was similar to other general population sexual behavior surveys (29-33), our samples

could have been biased in that the highly sexually active subpopulation may have avoided the survey. However, our experience with a nationwide survey of students from 30 universities in 1999 using a similar questionnaire showed little association between the answers to the questions related to sexual behaviors and the response rates that ranged between 16.4-100% (34). Finally, although the present study strongly suggests that oral sex may play an important role in the STI epidemic, it is possible that oral sex may be a marker related to sexual networks or other risks that were not captured in the present study.

Despite these limitations, the results of this study are important in showing that STI patients have diverse occupational backgrounds and are highly educated in Japan. It is also important to note that STI risk is universal, present not only in paid partnerships but also in casual and regular partnerships. Oral sex was just as much of a risk factor as vaginal sex. These findings should be translated into a socially and culturally appropriate STI/HIV prevention program in Japan. A particular focus of prevention should be placed on oral sex, as an oral sex industry has markedly proliferated in Japan during the last decade. This change may further spread STIs and thereby pave the way to an HIV epidemic in Japan. Finally it should be noted that 1999 is the middle of the period when Japan has experienced a dramatic increase in the sexual experience rate among teenagers, a sharp decline of domestic condom sales and the increases in STI and HIV infections (35). It is therefore possible that importance of the risk factors identified in the present study might have been intensified.

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