Published in final edited form as:
Int J STD AIDS. 2008 July ; 19(7): 455–458. doi:10.1258/ijsa.2008.007325.

The prevalence of chlamydial infection in Estonia: a population-based survey

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Summary

The aim of this study was to estimate the prevalence of *Chlamydia trachomatis* infection among Estonian men and women by a cross-sectional study based on the screening of a probability sample of the residents of Tartu using participant-collected, mail-delivered testing for *C. trachomatis* complemented with the self-administered questionnaire. Full participation as defined by returning both the questionnaire and specimen was 34% (*n* = 479; 95% confidence interval [CI] 32–37%). Study participation was 40% (*n* = 560; 95% CI 37–43%) for subjects returning either or both the study questionnaire and specimen. After weighing the population distribution, the prevalence estimate for the age group of 18–35 years was 5.4% (95% CI 3.0–7.5%), 6.9% (95% CI 3.6–10.3%) among women and 2.7% (95% CI 0.3–5.0%) among men. The number of sexual partners in the past 12 months was the strongest predictor of infection.

Keywords

Chlamydia trachomatis; chlamydia; prevalence; screening; Estonia

INTRODUCTION

The leading cause of bacterial sexually transmitted infection (STI) in industrialized countries is *Chlamydia trachomatis* (chlamydia).[1] Because most infections are asymptomatic2, the majority of infections remain undiagnosed.3 Despite the availability of effective treatment for a curable condition that can be identified through screening or case-finding, the morbidity and sequelae of chlamydia continue to dramatically impact the health of both women and men. In addition, bacterial STIs serve as biological cofactors that facilitate HIV transmission.4 Public health experts have noted that chlamydia treatment during the

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detectable, preclinical phase can reduce both short-term and long-term morbidity.[5,6] While controversial, it is widely believed that screening is an important component to prevent the adverse outcomes related to chlamydial infection.[6]

Estonian infectious disease surveillance is based on mandatory universal notification to the Health Protection Service for selected infections (including chlamydia). Reporting policies and procedures has been stable for the past three decades. However, screening for chlamydia (limited to the antenatal population) has been implemented over the past decade. Otherwise, testing for chlamydia is primarily conducted only on symptomatic patients seeking care at STI (dermatovenerology) clinics. Chlamydia is the leading bacterial STI in Estonia, and the estimated incidence of genital chlamydial infection in 2005 based on surveillance data was 188/100,000 population, an incidence that is comparable with other European countries.1 The incidence was highest (933/100,000) among those who are 20–24 years of age. Most reported chlamydial infections are among women, and this proportion has increased because of targeted screening in antenatal clinics from 66% in 1999 to 81% in 2005.9 While much is known about the incidence of diagnosed chlamydia, the true prevalence is unknown and proxies for prevalent infections must be utilized. For instance, the rate of ectopic pregnancy in Estonia is high and has increased during the last decade (15 per 1000 pregnancies in 1996 to 20 per 1000 pregnancies in 2006).7 Local studies suggest a high rate of post-inflammatory infertility, and in one laparoscopic study, signs of chronic genital infection were detected among 63–80% of infertile female patients.8 Studies recently conducted in Estonia describe a high rate of risky sexual behaviours and inadequate knowledge regarding prevention of disease transmission.9–11

This paper reports results of a study to estimate the prevalence and risk factors for chlamydial infection among Estonian men and women.

MATERIALS AND METHODS

Participants

Approval was obtained from the Ethics Review Board of the University of Tartu, Estonia. For the purpose of sample size calculations and based on a review of the literature, we assumed the overall *C. trachomatis* prevalence among the study population to be 5% with the margin of error for prevalence to be 2%. Taking into account the range of response rates (22–70%) reported for randomly selected, population-based home-sampling of STIs in published studies[12 – 15], the estimated sample size was 1690 persons.

A stratified (age, gender) random sample of a total of 1690 persons (845 women and 845 men) aged 18–35 was abstracted from the Estonian Population Registry's list of Tartu county residents (which includes both residents of Tartu city and residents of rural areas around the city). A random number generator was used to select the study participants from the approximately 51,000 individuals who met these eligibility criteria.

Study procedures

The study conducted from September 2005 to May 2006 consisted of an outreach-screening programme via questionnaire and participant-collected, mail-delivered testing for chlamydia. Each participant was mailed a package containing a specimen collection kit (urine for men and vaginal swab for women), collection instructions and an informed consent form attached to a 35-item questionnaire. Home-collected specimens were mailed directly to the laboratory, in pre-stamped, pre-addressed envelopes. Study procedures complied with local regulations regarding mailing of biological materials. The self-administered questionnaire took 10–15 min to complete, and participants were directed to

send completed forms to the study staff in a pre-stamped, pre-addressed envelope. The study subjects did not receive any financial incentives for participation.

Treatment of cases

In case of a positive result, patients were advised to be treated by their regular provider or by a dermatovenerologist of the study team working at the Dermatology/STI clinic. A letter or an email (depending on the participant's preference) containing the *C. trachomatis* test result was sent to participants to give to their provider of choice.

Measurements

The self-administered questionnaire solicited the following information: demographic variables (age, gender, marital status, level of education), sexual behaviour (whether they had been sexually active, age of first sexual contact, number of sexual partners), contraceptive and condom use, current urogenital symptoms, history of sexually transmitted diseases, and health-care utilization, particularly for STI diagnosis and treatment.

Possible selection bias between participants (those who returned a specimen and/or questionnaire) and non-participants (those who refused or did not respond) was assessed by comparing the two groups according to basic demographic variables from the population registry available for all invited people (age, sex, residence, ethnicity/mother tongue).

Laboratory testing

All the polymerase chain reaction (PCR) testing was done in Quattromed HTI Laboratory (www.quattromed.ee). Nucleic acid amplification testing (NAAT) PCR was used to detect *C. trachomatis* in self-collected samples (men: first voided urine; women: vaginal swab) submitted to the laboratory by mail. (Leakage occurred with one specimen, and testing was therefore impossible.)

The vaginal and urethral swabs or urine were stored for a maximum of three days at 4°C prior to DNA extraction. The material from swab specimens was suspended in phosphate-buffered saline (PBS) and collected by centrifugation at 16,060 *g* for 20 minutes. The supernatant was discarded and the pellet was resolved in PBS. Six millilitres of urine was centrifuged at 16,060 *g* for 20 minutes and the pellet was resolved in PBS after a washing step with PBS. DNA was extracted using high pure PCR Template Preparation Kit from Roche Molecular Biochemicals (Mannheim, Germany) according to manufacturer's instructions. *C. trachomatis* was detected, as described by Khan and Potter[16], using Eppendorf Mastercycler (Hamburg, Germany). PCR products were detected by ethidium bromide-stained agarose gel electrophoresis. The positive results for *C. trachomatis* were additionally confirmed using *artus C. trachomatis* TM PCR Kit (Qiagen, Hamburg, Germany) with ABI PRISM 7900HT Sequence Detection System (Applied Biosystems, Foster City, CA, USA). Only samples reactive with both assays were considered to be positive for *C. trachomatis*. Of note, the *artus C. trachomatis* TM PCR Kit was not affected by the 277 base pair deletion in the region of cryptic plasmid (a deletion that has lead to false-negative *C. trachomatis* results with several commercially available molecular diagnostic detection systems).[17]

Statistical analysis

The response proportion was computed as the total number of returned questionnaires/ specimens divided by the number sent to the randomly selected study population. This estimate was computed both for all mails sent and for those who actually received the packet. The prevalence of genital chlamydial infection was calculated by the number of cases divided by the number of submitted specimens. Weighted estimates of population

prevalence were computed to adjust for the stratified sampling utilized in the study design. Differences in characteristics between participants and non-responders and associations between prevalence and several characteristics were analysed using the chi-square test or unpaired *t*-test. All analyses were performed with SAS statistical software (version 9.1).

RESULTS

Response rate

Study invitations were received by 83% (1398/1690) of the targeted sample. A total of 292 individuals could not be reached because the packet was undeliverable (e.g. moved, wrong address). These people were excluded from analysis. A total of 560 men and women participated: 479 returned both questionnaire and specimen, 73 only the questionnaire and eight only the specimen. Of the 1398 participants who received the study packet, 34% (n = 479) returned both the questionnaire and specimen showing full participation, and 40% (n = 560) returned either, or both the study questionnaire and specimen.

Those who returned the questionnaire or specimen (n = 560) were compared with those who did not (n = 838) use population registry data for age, gender, residence (urban/rural) and ethnicity. There was no statistically significant difference in response proportion according to age or ethnicity/mother tongue. However, differences in response proportions reached statistical significance for gender (women vs. men: 48% [345/722]) and 32% [215/676], respectively, $P < 0.001$), and residency (rural vs. urban: 46% [170/370]) and 38% [390/1028], respectively, $P = 0.01$).

Participants

Respondents ranged in age from 18 to 35 years (mean 26.9, SD 5.6). Two out of three participants were either married (26%) or living with a sexual partner (40%). Two-thirds (59%) of participants had completed over 12 years of education (at least some posthigh school education). Most participants were employed (56%), in school (18%) or both (12%); 13% were neither employed nor in school. Most of the sample (85%) reported that they were ethnic Estonians and 15% reported a Russian ethnic background. Ninety percent of the participants were covered by state health insurance, and 65% of the participants had consulted their own family physician (71% of women and 55% of men) within the last year. With respect to contraceptive use among those participants who (who's partner) does not intend to conceive (502/552; 91%): 29% reported using condoms, 29% hormonal contraception, 10% intrauterine device and the rest (34%) relied on other methods, i.e. withdrawal and vaginal flushing (Table 1).

History of STI and current urogenital symptoms

History of ever having a STI diagnosis by a physician was reported by 21% of the participants and 32% were tested for STI within the last 12 months. Overall, 38% of respondents reported current urogenital symptoms: 54% of women (164/302) and 11% of men (19/177). Among the women with urogenital symptoms, 80% reported vaginal discharge, 33% pelvic (low abdominal) pain and 6.7% genital ulcer; among the men with urogenital symptoms, 63% reported genital ulcers and 47% either discharge from the urethra or painful urination.

Sexual behaviour

Thirty-four (7.1%) respondents were sexually inexperienced. Of the sexually experienced, the mean age of sexual debut was 17.6 years (range 16–19). Within the last year, most participants reported one partner (71%) while 23% reported two to five sexual partners. Men were more likely than women to report more than one partner (31% vs. 23%, $P = 0.0004$).

The majority of the respondents (84%) had a current primary partner. Women were more likely to be married or in a cohabiting partnership (71% vs. 58%, $P = 0.0007$).

Prevalence of chlamydial infection

The prevalence of chlamydia in the sample (25 positive results) was 5.2% (95% confidence interval [CI] 3.4–7.7%): 6.0% (95% CI 3.5–9.4%) among women and 4.0% (95% CI 1.6–8.1%) among men.

After weighing for the population distribution, the prevalence estimates for the age group of 18–35 years were as follows: overall 5.4% (95% CI 3.0–7.5%); 6.9% (95% CI 3.6–10.3%) among women and 2.7% (95% CI 0.3–5.0) among men.

The number of sexual partners in the past 12 months was the strongest predictor of infection. Participants who had two or more sexual partners had statistically higher prevalence (11.8%) when compared with those had one sexual partner (3.8%, prevalence ratio = 3.1; 95% CI 1.5–6.6, $P = 0.002$). Small samples sizes limited our ability to assess any association between chlamydial infection and demographic factors, healthcare factors or urogenital symptoms.

DISCUSSION

This is the first study to report the prevalence of *C. trachomatis* infection in a former Soviet Union country. The observed prevalence was 5.2% among participants of 18–35 years, which is consistent with the results presented from the neighbouring European countries. Low*et al.*[14] reported 3.2% prevalence of chlamydia in a study implementing home-testing and randomly selected participants from the urban general practitioner practices (UK). Andersen *et al.*[15] from Denmark reported prevalence of 6.5% among women and 5.9% among men aged 21–23 years, randomly selected from the county's health service register and invited to submit home-obtained samples via mail.

This study had several limitations. While the cross-sectional study design does not allow us to establish a causal relationship, our goal was to estimate prevalence and factors related to prevalence. The degree to which the study is representative of the larger population is influenced by the low response rate and potential selective factors associated with response. However, this response rate was similar to that seen in recent studies.[14,15,18] To evaluate the effect of selection bias, we collected demographic information from all non-respondents. The probability of not responding was greater for men, a phenomenon described in several previous studies. A second limitation was the fact that a sizable proportion of female study participants had current urogenital symptoms, and those who responded may have done so because they were explicitly seeking chlamydia testing for an extant symptomatic condition. Thus, the prevalence of chlamydia reported here may over-represent the true rate of infection in the source population. The association between chlamydial infection and symptoms suggests that home-sampling may well serve as opportunistic screening. An issue to be considered in screening studies is the use and possible abuse of screening tests. In low-prevalence settings, even excellent tests have poor positive predictive value.[19] To minimize the likelihood of a false-positive, a positive NAAT test was based on double-testing for *C. trachomatis* using two different NAAT tests (primers). Thus, while it is reasonable to assume that the prevalence estimates from this study are somewhat inflated because of selective participation, the estimate is likely better than that based on traditional surveillance data. Finally, the sample size was insufficient for further stratification.

In European countries, genital chlamydial infection is now among the most commonly diagnosed bacterial STI, and this diagnosis has been on the rise since the mid-1990s.[1] Both

surveillance and clinical case notification data suggest a disproportionate disease burden among women in Estonia, as well as in many other countries.[1,9] However, opportunistic screening often introduces bias in the data collected by national passive surveillance and clinical case notification systems. Recent population-based surveys in Scandinavia, the UK and the USA have consistently shown similar prevalence of chlamydia among heterosexual men and women.[14,15,20] Men are an important reservoir of infection for women, and men also suffer health consequences from chlamydial infection.[21] As such, men should also be targeted for chlamydial screening and treatment. Recently, in the USA, the CDC has recommended chlamydial screening for specific higher risk groups of men.[22]

Pinpointing target groups for chlamydial screening remains a challenge. Most infected individuals are asymptomatic. Population-based studies to identify risk factors for chlamydia have not identified specific factors, other than young age, that would more efficiently target screening. The majority of our study participants had consulted their family physician within the last 12 months of the study. Family-physician practices could thus provide good opportunistic screening access for both men and women. A strategy of using mailed samples as an adjunct to screening during health visits may enhance access to STI testing. As also suggested by earlier studies[14] mixed models of chlamydial screening, such as specimen collection by a health-care provider or self-obtained, and active or opportunistic screening should be evaluated to determine which model delivers consistently higher uptake than either alone. Effective methods for identifying and treating those who are infected with chlamydia need to be developed and evaluated in Estonia and similar countries.

Acknowledgments

This study was supported by a Grant No. R01 TW006990 from the Fogarty International Center and Grant No. 3 D43 TW00233 from the Fogarty International Center, NIH, USA.

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Table 1

Sample characteristics of study participants

Characteristics	Men (%)	Women (%)	Total (%)
No.	209	343	552
Sociodemographics			
Age			
< 20	23 (11.0)	23 (6.7)	46 (8.3)
21–24	58 (27.8)	117 (34.1)	175 (31.7)
25–	127 (60.8)	202 (58.9)	329 (59.6)
Marital status			
Married	51 (24.4)	88 (25.7)	139 (25.2)
Cohabiting	71 (34.0)	147 (42.9)	218 (39.5)
Others	4 (1.9)	18 (5.2)	22 (4.0)
Single (never married)	83 (39.7)	90 (26.2)	173 (31.3)
Health			
Heard about chlamydia before			
Yes	134 (64.1)	290 (84.5)	424 (76.8)
Visiting family physician within last 12 months			
Yes	115 (55.0)	245 (71.4)	360 (65.2)
Having state health insurance			
Yes	186 (89.0)	314 (91.5)	500 (90.6)
Receiving antibiotics within last four weeks			
Yes	19 (9.1)	51 (14.9)	70 (12.7)
Sexually transmitted infections			
Self-reported history of STI			
Yes	30 (14.4)	86 (25.1)	116 (21.0)
Sexually transmitted infection symptoms			
Men (urethral pain and/or discharge)			
Yes	12 (5.7)	NA	NA
Women (low abdominal pain, contact bleeding)			
Yes	NA	184 (53.6)	NA
Sexual behaviour (among sexually experienced)			
No.	188	326	514
Age at first sex			
<16 years	32 (17.0)	56 (17.2)	88 (17.1)
Number of sexual partners in the last 12 months			
1	118 (62.8)	240 (73.6)	358 (69.6)
2–5	49 (26.1)	72 (22.1)	121 (23.5)
≥6	9 (4.8)	0 (0.0)	9 (1.8)
Condom use (last sexual intercourse)			
Yes	64 (34.0)	86 (26.4)	150 (29.2)