

Factors associated with repeat symptomatic gonorrhea infections among men who have sex with men, Bangkok, Thailand

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Disclaimer

The findings and views presented in this presentation are those of the author and do not necessarily represent those of the US Centers for Disease Control and Prevention.

Background

- *Neisseria gonorrhoea* (NG) infection may increase the risk of HIV transmission¹⁻³
- Gonococcal infection is concentrated in specific communities⁴⁻⁵ and subgroups of men who have sex with men (MSM) are at high risk for gonorrhoea infection^{3, 6, 7}
- Gonorrhoea treatment is complicated by the ability of NG to develop resistance to antimicrobials, which limits the options for effective treatment and control of the disease^{4, 8, 9}
- Decreasing cephalosporin sensitivity among NG isolates was reported from the Gonococcal Isolate Surveillance Project, which found that MSM are vulnerable to the emerging threat of antimicrobial-resistant NG¹⁰
- Overall, around 6% of male and female patients receiving care in the UK were diagnosed with a repeat episode of NG within 6 months, and the majority (90%) of individuals diagnosed with NG reinfection were symptomatic¹¹
- High prevalence of asymptomatic NG infection (7.5%), a predominance of rectal site infections and substantial diversity in correlates of infection between mucosal sites, were reported from MSM in Bangkok, Thailand⁶

Objectives

Among MSM enrolled in the Bangkok MSM Cohort Study (BMCS):

- To determine prevalence of rectal and urethral NG infection at baseline
- To describe incidence of symptomatic NG infection
- To evaluate baseline factors associated with repeat symptomatic NG infections during follow-up

Methods

- Study design: Prospective cohort study with 4-month interval for 3-5 years
- Study population

Eligibility criteria:

- Thai male aged ≥ 18 years
- Residing in the Bangkok metropolitan area
- Reporting penetrative oral or anal sex with another man in the past 6 months
- Available to participate in a 4-month follow-up visit

Recruitment methods:

- Convenient sampling from venues, Internet, a male sexual health clinic, and through outreach workers and friends

Methods

- Inclusion criteria for analysis :
 - Men who had rectal and/or urethral specimens collected at enrollment
 - Available for at least one follow-up visit for the calculation of incidence rate and factors associated with number of symptomatic NG infections during follow-up

Methods

- At baseline:
 - Rectal swab, pharyngeal swab and first-void urine were collected for *Chlamydia trachomatis* (CT) and NG infection using nucleic acid amplification testing (NAAT) and Gram stain (for NG only)
 - HIV testing
 - Physical examination
 - Assessment of behaviors using computer-assisted self-interview (ACASI)
- At follow-up visit:
 - Symptomatic participants (i.e. men with urethral or anal discharge, urethral pain and rectal pain) were tested for NG and CT infection by NAAT and Gram stain from rectal or urethral specimens
 - HIV testing, ACASI and physical examination
- At unscheduled visit:
 - Physical examination if participants had signs or symptoms consistent with CT or NG infection

Methods

- CASI questionnaire on risk behaviors in the past 4 months administered every 4 months. Key questions included:
 - Baseline: socio-demographic characteristics, history of HIV testing, history of diagnosis with Sexually Transmitted Infections
 - Baseline and follow-up visit: use of recreational injectable/oral/inhalant drug to increase pleasure and/or sexual pleasure and sexual behaviors
- Men diagnosed with NG infection at any visit were treated using regimen recommended by the Thailand National Guidelines*:

First line: 250 mg IM ceftriaxone

Second line: 400 mg oral single dose

*Routine empirical treatment for CT also recommended

Laboratory testing

- First-void urine and rectal swabs (Amplicor[®] STD Swab Collection and Transport set) were tested for CT and NG by NAAT (Roche Amplicor[®], Roche Diagnostics, Branchburg, NJ, USA) and Gram stain (for NG only)
- HIV testing on oral fluid using OraQuick[®] HIV-1/2 Rapid Test (OraSure Technologies, Bethlehem, PA, USA). If reactive, confirmed with three rapid tests on blood:
 - Determine[™] HIV-1/2 (Abbott Laboratories, Tokyo, Japan) or Determine[™] HIV-1/2 (Alere Medical, Chiba, Japan)
 - DoubleCheck[™] II HIV 1&2 (Organics, Yavne, Israel), replaced after 02/2011 by SD-Bioline HIV-1/2 3.0 (Standard Diagnostics, Kyonggi-do, South-Korea) and replaced after 01/2012 by DBCheck Gold Ultra HIV-1/2 (Organics, Yavne, Israel)
 - Capillus[™] HIV-1/HIV-2 (Trinity Biotech, Jamestown, NY, USA), replaced after 11/2008 by Core[™] HIV-1/2 (Birmingham, UK)

Confirmation requires that all 3 tests are reactive

Statistical Analysis

- NG and CT prevalence at baseline was calculated as the proportion of men that tested positive by NAAT and/or intracellular Gram positive diplococci found by Gram stain, divided by the number of men tested
- We calculated symptomatic NG incidence per 100 person-years (PY) with exact Poisson 95% confidence interval (CI); follow-up time through December 2014
- We determined factors associated with number of symptomatic NG infection using Poisson regression with robust standard error
- Time independent exposures (baseline) with p -value ≤ 0.10 were entered into multivariate model; likelihood ratio test was used to determine the final models
- We performed all analyses using STATA (Version 12, Stata Corp., College Station, Texas, USA)

Results

- At baseline:
 - Of 1,744 men enrolled during 2006-2010, 1 (0.1%) had no specimen collected and 1595 had both rectal and urethral specimen collected
 - Rectal NG prevalence was 6.1% (98/1595)
 - Urethral NG prevalence was 1.8% (29/1595)
- At follow-up visit:
 - 145 men were lost to follow-up (i.e., never returned for any follow-up visit after enrollment by September 30, 2014)
 - 1439 men were available for: \geq one follow-up visit; no NG infection detected by NAAT/Gram stain at enrollment; and available for both rectal and urethral specimens, included in the longitudinal analysis

Results

Table 1: Participants characteristics, N=1439

	n	%	Median (IQR)
Age (years)			26 (22, 30)
18-24	563	39.1	
≥25	876	60.9	
Education level			
Primary or less	34	2.4	
Secondary/technical/vocational	736	51.1	
University/higher	669	46.5	
Sexual identity			
Bisexual	235	16.3	
Transgender woman	45	3.1	
Homosexual/gay	1154	80.2	
Heterosexual	5	0.3	
Enrollment period			
2006-2008	1041	72.3	
2009-2010	398	27.7	

Results

- Repeat symptomatic NG infections during follow-up:
 - 119 men had symptomatic NG infection at any follow-up visit (incidence 2.1 per 100 Persons-Years: 95% CI 1.8-2.6)
 - Of 119 men with symptomatic NG infections, 81.5% (97/119) were urethral infections, 17.6% (21/119) were rectal infections and 0.8% (1/119) were both the urethra and the rectum
 - Repeat symptomatic NG infections were 40.3% (48/119) of participants: 68.7% (33/48) at the urethral site; 6.2% (3/48) at the rectal site; and 25.0% (12/48) were between the urethra and rectum
 - Of 48 men with repeat symptomatic NG infection, 50.0% (24/48) had 2 infections; 27.1% (13/48) had 3 infections; 8.3% (4/48) had 4 infections; 8.3% (4/48) had 5 infections; 2.1% (1/48) had 6 infections and 4.2% (2/48) had 7 infections
 - 13.4% (16/119) had repeat symptomatic NG infections within six months
Median time between the first 2 infections was 294 days (IQR: 169-461 days)

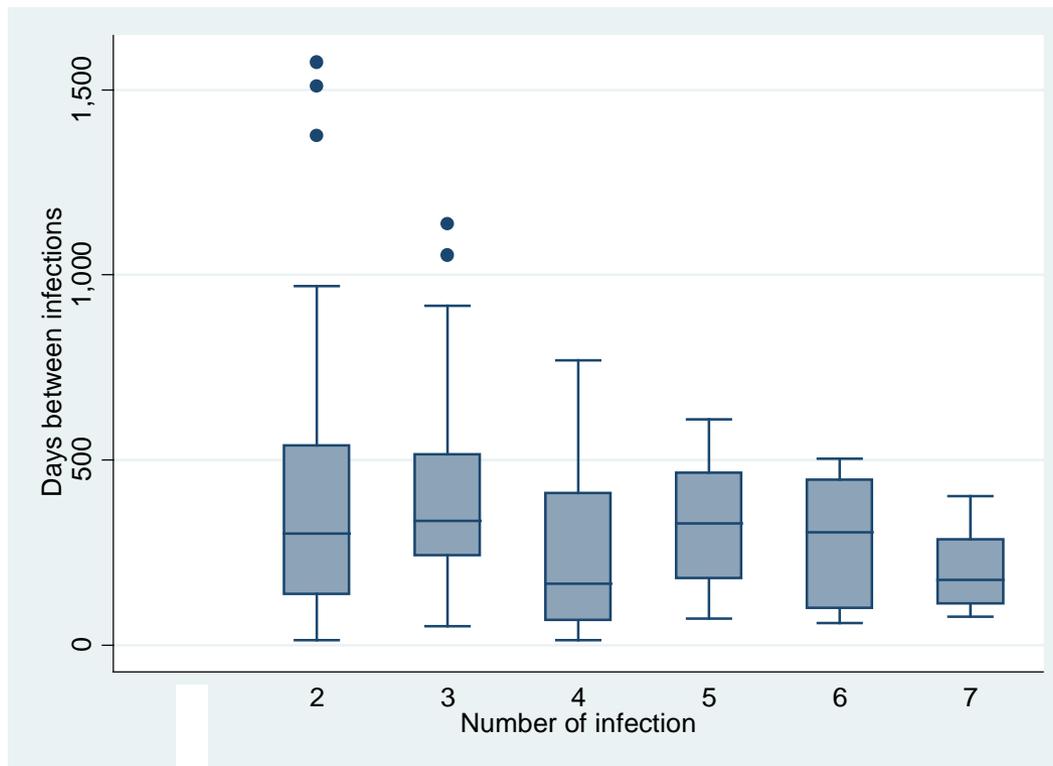


Figure 1: Number of Repeat Symptomatic Infections and Number of Days Preceding and Following Infection, Thai MSM enrolled in the BMCS 2006-2010, Bangkok, Thailand

Table 2: Risk factors significantly associated with number of symptomatic NG infections among a cohort of MSM participated in the BMCS, Bangkok, Thailand

Characteristics	Number of symptomatic NG infections*	
	Adjusted Incidence Rate Ratio (Adjusted IRR)	95% CI
Period of enrollment		
2006-2008	2.5	1.5-4.3
2009-2010	Ref.	
History of HIV testing		
Ever and know the result	1.0	0.7-1.6
Ever but and do not know the result	2.8	1.2-6.7
Never tested	Ref.	
History of previous STI diagnosis		
Ever	2.9	1.8-4.4
Never	Ref.	
Prevalent CT infection at baseline		
Yes	2.2	1.4-3.6
No	Ref.	
*NAAT or Gram stain		

Conclusions

- Over a third of men with symptomatic NG infection had repeat infection
- Symptomatic repeat NG infections was associated with other STIs
- Specific prevention efforts might effectively be targeted to MSM who are diagnosed with NG and/or CT infection including
 - follow-up evaluation in 3 months for repeat NG and/or CT
 - increase access to same day HIV test result
 - strengthen post-HIV test counseling

Limitations

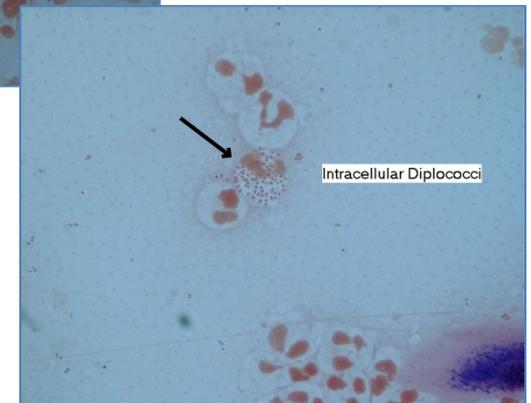
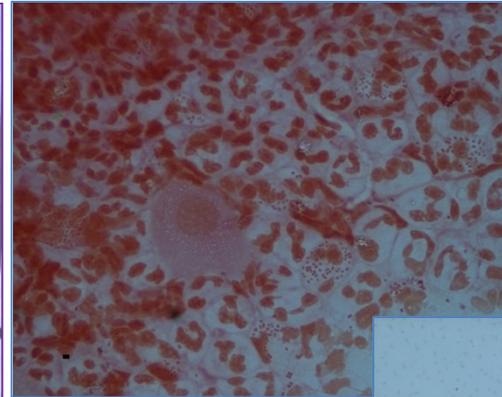
- Incidence rate reported here is likely an underestimation given we tested NG infection in men who experienced symptoms
 - Many men may have had asymptomatic infection and might not have been captured
- We did not include dysuria in the definition of symptom
- We did not assess if the repeat symptomatic NG infection was reinfection or persistent infection

Recommendations

- Continued surveillance for NG and CT infection in at risk MSM is needed
 - Routine culture and antimicrobial testing would be important to assess treatment failures as a reason for repeat infection
 - Routine testing for cephalosporin susceptibility in MSM who develop repeat symptomatic NG infections are needed
- Routine follow-up after NG and CT needed to assess for repeat infections
- Expand coverage of HIV counseling and testing

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Silom Community Clinic staff (left) , gram stain for rectal NG infection (middle) and gram stain for urethral NG infection (right)

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