



Screening for Urethral, Rectal and Pharyngeal Gonorrhea & Chlamydia among Asymptomatic Male Adolescents and Young Men who have Sex with Men

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Abstract

Purpose: Urban young men (13-25 years old) who have sex with men (YMSM) are at high risk for sexually transmitted infections (STIs). Centers for Disease Control and Prevention (CDC) recommendations are to screen asymptomatic MSM for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (GC) based on sexual history. However, this approach misses asymptomatic non-genital infections in men who do not disclose or are not asked about sexual behavior. Our study aimed to determine prevalence of asymptomatic pharyngeal, rectal and genitourinary chlamydia and gonorrhea infections in YMSM in St. Louis, MO.

Methods: Asymptomatic YMSM (13-25 years old) presenting for STI/HIV testing to a free community based youth center in St. Louis, Missouri, between April 1, 2012 and March 31, 2015 were offered urethral, rectal and pharyngeal chlamydia and gonorrhea testing. A screening event included Nucleic Acid Amplification Testing (NAAT) at all three sites.

Results: 412 YMSM had triple screening. 141 (34.2%) youth had either chlamydia and/or gonorrhea infections. 74 youth had gonorrhea, 45 had chlamydia and 22 were positive for both in the same testing event. CT was most often found in the rectum, 52/412 (12.6%). GC was most often found in the pharynx 54/412 (13.1%), followed by the rectum 50/412 (12.1%). Urine testing alone would have missed most infections with CT (74.6%) and GC (82.3%).

Conclusion: The rate of GC and CT infections at non-genital sites is high in asymptomatic, YMSM in our community. Genitourinary screening alone leaves many of these men with untreated STIs and underestimates infection burden. These findings suggest triple testing is important to identify asymptomatic young MSM with GC and CT. More study in other areas may add evidence to change CDC guidelines and have YMSM opt out of triple testing as opposed to using sexual history to opt in to non-genital testing.

Keywords

Chlamydia trachomatis (CT), Neisseria gonorrhoeae (GC), CDC (Centers for Disease Control and Prevention), Sexually transmitted infections (STIs), Men who have sex with men (MSM), Human immunodeficiency infection (HIV)

Disease Control and Prevention (CDC) for all reportable conditions, reflecting an increase of 8% compared to 2010 [1]. CDC's recent estimates suggest 20 million new STI cases occur in the United States each year. These infections cost the American healthcare system nearly \$16 billion in direct medical costs alone and almost half of these infections occur in young people age 15 to 24 years [2].

Current estimates of CT and GC prevalence are based mainly on urethral testing; however, both CT and GC can also infect the mucosal surface at non-genital sites including the oropharynx and the rectal mucosa. Prevalence estimates vary depending on the population and site being screened [3]. In the adult MSM population, the prevalence of CT varies from 1.5-3.5% (pharyngeal) to 5-15% (rectal) while that of GC varies from 5-15% for both, pharyngeal and rectal infections [4-6]. Pharyngeal and rectal infections typically occur without concomitant urethral infection [7,8]. Moreover, these non-genital infections are found to have strong association with an increased risk of acquiring HIV infection. In one study, a history of two rectal infections with either GC or CT was associated with an 8-fold increased risk of acquiring HIV infection in the following two years [9].

However, there is limited data of non-genital GC/CT in the adolescent/young adult (ages 13-24 years) population of MSM which accounts for more than half of STIs and newly diagnosed HIV infections each year [1]. Currently, CDC recommends CT/GC screening based on sexual history--at least annual screening with urine nucleic acid amplification testing (NAAT) for those MSM who report insertive intercourse and rectal and/or pharyngeal NAAT are recommended for those men who report receptive oral or anal intercourse. More frequent urethral and rectal CT/ GC screening and pharyngeal GC screening is to be considered for those with multiple anonymous partners, MSM who have sex in conjunction with illicit drug use or whose sex partners participate in these activities and recommends that they be screened more frequently [10]. However, despite the CDC recommendations, few MSM report having received the appropriate testing in non-genital sites [11,12].

For detection of genital as well as non-genital GC and CT infections, NAAT are shown to be more sensitive than culture [12,13]. However, pharyngeal and rectal NAAT is not Food and Drug Administration (FDA) approved for use so each laboratory is

Introduction

Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (GC) infections are the two most commonly reported sexually transmitted infections (STIs) in the United States. In 2011, CT infections accounted for the largest number of cases reported to the Centers for

Citation: Ali F, Kaushik GN, Carr ND, Hayes E, Plax KL (2016) Screening for Urethral, Rectal and Pharyngeal Gonorrhea & Chlamydia among Asymptomatic Male Adolescents and Young Men who have Sex with Men. J Fam Med Dis Prev 2:046

Received: August 20, 2016; **Accepted:** November 04, 2016; **Published:** November 08, 2016

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required to validate its own NAAT [4,14]. This situation may create further barriers to pharyngeal and rectal testing for MSM.

Our objectives in this cross sectional study were: (1) to evaluate the prevalence of asymptomatic rectal, urethral, and pharyngeal CT and GC infections in a young MSM population seen at an urban youth drop-in center; (2) to assess the rates of infections missed by urine specimens alone.

Methods

Study setting and population

This study was conducted at The SPOT (Supporting Positive Opportunities for Teens) [15], a drop-in center that provides free health and social services for youth 13-24 years of age, in the city of Saint Louis, Missouri. The SPOT, established in 2008 has served over 11,000 patients as of September 2015. The SPOT has trained staff to be inclusive of the spectrum of gender and sexual orientation and 12% of the population served identifies as LGBT. This study was approved by the Institutional Review Board of the Washington University School of Medicine.

Between April 01, 2012 and March 31, 2015, urethral, pharyngeal and rectal GC and CT screening was offered to all self-reported MSMs who presented for STI screening. MSM was defined as men who reported sex with men or both men and women in a structured clinical interview. In addition, youth were asked to self-report on

sexual orientation and MSM identified as gay, straight, bisexual and unsure. In our clinic MSM clients are encouraged to undergo testing every 90-180 days, based on risk factors or presence of past positive STI. Asymptomatic status was also determined in a clinical interview, and was defined as absence of discharge from the penis or anus, rashes or sores, dysuria, or pharyngeal, penile or anal discomfort. These questions were asked of all patients and boxes for symptoms were available for the provider to check in the electronic health record computer visit form. A total of 465 youth were tested in the study duration. All symptomatic patients (n = 53) were excluded from the analysis. For the present analysis a screening event was defined as an asymptomatic MSM who had testing at all three sites on the same day. In the study period 197 youth presented for more than one screening event. But only the initial presentation for screening during the study period was included in the analysis. Demographic and sexual risk behavior information was also collected through standardized visit forms in our electronic health record.

All individuals were informed about their test results, and, if positive, free STI treatment was provided. Appropriate STI reports consistent with Missouri law were made to the St. Louis City Health Department.

Specimen collection

Urethral testing was performed using urine specimens. Pharyngeal and rectal specimens were collected during the clinic visit using

Table 1: Demographics of the youth screened.

Characteristics	Screen negative N = 271	Screen positive N = 141	Total screened N = 412	P -value
Age (Years)				
14-17	33 (12.18%)	15 (10.64%)	48 (11.65%)	0.45
18-22	176 (64.94%)	94 (66.67%)	270 (65.53%)	
23-25	62 (22.88%)	32 (22.70%)	94 (22.82%)	
Race				
African American	173 (63.84%)	101 (71.63%)	274 (66.50%)	0.49
Caucasian	68 (25.09%)	29 (20.57%)	97 (23.54%)	
Multiracial	15 (5.54%)	8 (5.56%)	23 (5.58%)	
Others	15 (5.54%)	3 (2.13%)	18 (4.37%)	
Education				
GED	14 (5.17%)	9 (6.38%)	23 (5.58%)	0.14
Not completed high school	38 (14.02%)	22 (15.60%)	60 (14.56%)	
High school graduate	61 (22.51%)	36 (25.53%)	97 (23.54%)	
In college	93 (34.32%)	49 (34.75%)	142 (34.47%)	
Graduated college	28 (10.33%)	11 (7.80%)	39 (9.47%)	
Missing/Not available	37 (13.65%)	14 (9.93%)	51 (12.38%)	
Housing				
With parent/ guardian	110 (40.59%)	58 (41.13%)	168 (40.78%)	0.22
With roommate	49 (18.08%)	33 (23.40%)	82 (19.90%)	
Alone	35 (12.92%)	12 (8.51%)	47 (11.41%)	
Homeless/Shelter/Transitional	26 (9.59%)	13 (9.22%)	39 (9.47%)	
School dorm	11 (4.06%)	5 (3.55%)	16 (3.88%)	
Missing	40 (14.76%)	20 (14.18%)	60 (14.56%)	
Gender				
Male	260 (95.94%)	135 (95.74%)	395 (95.87%)	0.70
Transgender (M to F)	11 (4.06%)	6 (4.26%)	17 (4.13%)	
Orientation				
Gay	205 (75.65%)	104 (73.76%)	309 (75.00%)	0.56
Bisexual	43 (15.87%)	27 (19.15%)	70 (16.99%)	
Straight	10 (3.69%)	2 (1.42%)	12 (2.91%)	
Unsure	13 (4.80%)	8 (5.67%)	21 (5.10%)	
HIV Status*				
Positive	34 (12.55%)	33 (23.40%)	67 (16.26%)	0.63
Negative	234 (86.35%)	108 (76.60%)	345 (83.01%)	
Unknown	3 (1.11%)	0 (0.00%)	3 (0.73%)	
Last 6 months partners				
≤ 5	196 (72.32%)	81 (57.45%)	277 (67.23%)	0.51
> 5	25 (9.23%)	20 (14.18%)	45 (10.92%)	
Not recorded	50 (18.45%)	40 (28.37%)	90 (21.84%)	

(%) are expressed as percentage of the total (N).

BD- probe-Tec swabs (Becton, Dickinson and Company, Sparks, MD). Pharyngeal samples were collected by clinicians swabbing the tonsillar pillars and posterior pharyngeal wall. Rectal specimens were self-collected by patients after instructing them to insert the tip of a swab completely into the anal canal. Specimens were kept in SDA transport media and stored at room temperature.

Laboratory assays

CT/GC NAAT was performed at the Center for Disease Detection (CDD) Laboratory located in Saint Antonio, TX. BD-Probe-Tec swabs and urine specimens were processed by the laboratory in accordance with the manufacturer's protocol (BD Probe-Tec™ ET System). The CDD laboratory validated the BD Probe-Tec (Strand Displacement method) assay on pharyngeal and rectal specimens in a manner consistent with recommendations from the CDC and the Association of Public Health Laboratories [6,16].

Statistical analysis

For our analyses, we included only asymptomatic MSM who had been screened for chlamydia and/or gonorrhea at all three sites, i.e. urogenital, rectum and pharynx. Testing site and infection events were used for analysis, such that for one infection, CT or GC, there could be one, two or three test sites that were positive. However, positive tests for both CT and GC at the same event were counted as two infections and reported as both. A T test analysis was used to evaluate significant differences between the screened positive and screened negative groups. All the analyses are descriptive and were performed using Microsoft Excel 2010 and IBM SPSS 21. T test, chi squared and p value were used for identifying statistical significance. Two sample t-test were done with statistical significance of 0.05%.

Results

In the three-year study period (April 2012- March 2015) 465 youth were screened. Of the 465 screened, data for 53 youth who were symptomatic at screening was not used for analyses. Table 1 provides the demographics of the youth. There were no statistically significant differences between infected and uninfected patients with regards to age, race, education, housing status and sexual orientation. Of note, 17% of the young men reported sex with women as well.

In the 3 years, 141 youth (34.2%) had infections of GC and/or CT identified. 74 youth had GC only, 45 youth had CT only and 22 youth were positive for both GC and CT at the same testing event. A positive test for CT was most often found in the rectum, 52/412 (12.6%). A positive test for GC was most often found in the pharynx 54/412 (13.1%), followed by the rectum 50/412 (12.1%) (Table 2). Of the 141 clients with an infection, 89 youth (63.1%) had a positive rectal test, compared to 31 (21.9%) with urogenital testing. Urethral testing was the least likely to be positive for either CT or GC. 78 % of youth with either infection would have been missed by urine screening alone. Urine testing alone would have missed 50/67 (74.6%) of the CT infections and 79/96 (82.3%) of the GC infections (Table 3). Most of the CT infections were diagnosed by rectal screening alone whereas rectal and pharyngeal testing diagnosed most of the

GC infections (Table 3). In patients who had a rectal CT infection, 7/52 (13.4%) were positive in their urine. Similarly, for patients with a positive rectal GC infection 10/50 (20%) had a positive urine test and for those youth with a positive pharyngeal GC infection 17/54 (31%) had a positive urine test.

Discussion

To our knowledge, this is the first study of urethral, rectal and pharyngeal screening for GC and CT infections, focusing solely on adolescent and young adult MSM. We found that non-genital sites harbor the most infections in this young MSM population, comparable to data from adult studies [8,17]. Nearly 4 out of 5 of these infections would be missed by relying on urine screening alone. We also found that although the CDC does not recommend routine pharyngeal testing for CT 1.7 % of our population had oropharyngeal CT [10].

The CDC recommends the MSM population have screening of genital as well as non- genital sites at 3-6 month intervals for those at highest risk, which includes MSM with multiple anonymous partners, who use illicit drugs or whose sex partners engage in this high risk behavior. In addition the CDC also calls for that screening to be done based on reported sexual history, namely receptive oral and anal intercourse [1]. However, self-reporting of sexual behavior, especially in youth, is developing and is influenced by social stigmatization and discrimination [18], which can then lead to missed screening opportunities. In addition healthcare practitioners are often inadequately trained and may feel uncomfortable in eliciting detailed sexual histories from patients [19,20]. We therefore set a low screening threshold for triple testing and offered it to all men who reported sex with men. As expected, we also saw that sexual orientation and sexual behavior are varied as young men reported sex with men in a clinical interview and identified across the spectrum in sexual orientation self-report. Our finding suggests that all youth MSM presenting for STI screening should have samples taken from all three sites regardless of sexual history and that prevalence for youth in our community was at the high end for adult reported data among MSM [17,21,22].

Apart from the risk of ongoing transmission of CT and GC infections, multiple studies have shown a significantly increased risk of HIV transmission associated with these infections, particularly with rectal CT and GC infection [23,24]. In particular, GC infection is recognized as one of the strongest and most consistent risk factors associated with HIV acquisition [25]. In 2011, 15-24 years old youth account for 41% of newly diagnosed HIV infections. [26] and while the overall rate of new HIV infections has declined in the United States, youth, young MSM have continued to experience a growth in HIV infections [27]. Improved STI screening may increase awareness among young MSM of their risk for STIs and HIV infection and encourage their engagement with evidenced based STI/ HIV prevention efforts, including pre-exposure prophylaxis (PrEP) [28,29]. In addition, the high prevalence of STIs indicates the need for new efforts and strategies to prevent HIV transmission in our community.

Table 2: Prevalence* of STI in the population on site of the test.

Prevalence	CT	GC	Coinfection**	Overall
Overall	16.26% (67/412)	23.30% (96/412)	5.34% (22/412)	34.22% (141/412)
Based on Urinary testing	4.13% (17/412)	4.13% (17/412)	0.73% (3/412)	7.52% (31/412)
Based on Pharyngeal testing	1.70% (7/412)	13.11% (54/412)	0.24% (1/412)	14.56% (60/412)
Based on Rectal testing	12.62% (52/412)	12.14% (50/412)	3.16% (13/412)	21.60% (89/412)

(*) Prevalence is prevalence of infection in the population.

(**) The numbers is subset of the CT and GC prevalence.

Table 3: Youth missed/Infections if we only used one site to test.

Percentage of youth missed/Infections	CT	GC	Overall
Based on Urinary testing	74.63% (50/67)	82.29% (79/96)	78.01% (110/141)
Based on Pharyngeal testing	89.55% (60/67)	43.75% (42/96)	57.45% (81/141)
Based on Rectal testing	22.39% (15/67)	47.92% (46/96)	36.88% (52/141)

Despite having superior sensitivity and specificity, current NAAT are FDA-approved only for genitourinary specimens. In order to use these methods for specimens from non-genital sites, laboratory validation is required [1]. The rapid turnaround time, the ability to test for both CT and GC in the same specimen using species-specific probes, and the elimination of difficult culture methods represent a significant step forward in the field of STI diagnosis. The possibility of false-positive results, particularly with pharyngeal gonococcal specimens may limit the use of NAAT, but its use in populations with a high prevalence of infection and an increased risk of HIV acquisition outweighs these limitations [30,31]. In one such report just one false positive was identified in the published literature [30]. In addition, GC culture can always be obtained if GC infection persists or there is concern for resistant infection or need for antibiotic resistance testing.

We recognize that our study has limitations. The testing was conducted in a single clinic site in St. Louis, MO so we may not be able to generalize the results. Testing of all three sites was only offered to men who self-reported sex with men. Sexual health data including the number of partners and symptoms was also self-reported so is susceptible to social desirability influences. Although CDC recommended, the screening method (NAAT) used is not FDA approved for non-genital specimens. However, the laboratory that performed testing in our study used a validation process consistent with CDC recommendations.

In conclusion, the rate of GC and CT infections at non-genital sites is extremely high in asymptomatic, young MSM tested in our community. Genitourinary screening leaves many of these men with untreated STIs and underestimates infection burden. These findings suggest triple testing is important to identify young MSM with GC and CT and further efforts are needed to make this method of testing more widely available and FDA approved. More studies are needed to determine how often the screening should be recommended.

Implications

These findings suggest triple testing is important to identify asymptomatic young MSM with GC and CT. More study in other areas may add evidence to change CDC guidelines and have YMSM opt out of triple testing as opposed to using sexual history to opt in to non-genital testing.

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