

## Clinical Aspects of Diagnosis of Gonorrhea and *Chlamydia* Infection in an Acute Care Setting

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**We found a 10.4% prevalence of unrecognized genital gonorrhea and *Chlamydia* infection among young adults of an urban emergency department. Intensified detection and treatment policies are needed to prevent continued transmission and complications of sexually transmitted infections.**

*Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections are the most common reported bacterial infections in the United States [1]. Many infections are asymptomatic [1–4], and if left untreated, chlamydial and gonococcal infections are major risk factors for pelvic inflammatory disease (PID), which increases the risk of infertility and ectopic pregnancy [3, 5]. Chlamydial and gonococcal infections also facilitate HIV transmission and acquisition [6–8].

Patients with sexually transmitted diseases (STDs) and their sequelae are often seen in emergency departments (EDs). In the 1992–1994 National Hospital Ambulatory Medical Care Survey ER supplement, 47% of all gynecologic presentations to EDs were diagnosed as genital tract infections (including PID, lower genital tract infections, and STDs) [9]. PID was the most common gynecologic diagnosis, resulting in an estimated 342,000 ED visits per year [9]. Ascertainment of STDs in ED settings is often suboptimal. In 3 retrospective studies that

linked clinical diagnosis to laboratory results, 42%–76% of patients for whom laboratory results were positive were not diagnosed at the ED visit, findings that are seen in urban and rural environments [10–12]. Furthermore, even after phone, mail, and public health follow-up, treatment could not be documented for 25% of the patients. Only 1 of the hospitals had a callback system in place for inadequately treated patients [11].

In 1997, Baltimore had the nation's highest urban rates of gonorrhea and syphilis. Previous epidemiological analyses by our group have documented that rates of STDs in the east Baltimore community adjacent to the Johns Hopkins Hospital are among the city's highest [13], and that there is a high prevalence of chlamydial and gonococcal infections among the population of the Johns Hopkins Hospital Adult ED. The objective of this study was to prospectively determine clinical and demographic characteristics of undiagnosed chlamydial and gonococcal infections in the ED setting. This information can be used to aid in the development of clinical recommendations for improved recognition and treatment of STDs in patients in urban ED settings.

**Methods.** The Johns Hopkins Hospital is a university teaching hospital and level 1 trauma center with ~48,000 annual visits; it is located in urban east Baltimore. The ED provides care to a socioeconomically disadvantaged and underinsured population. A total of 76% of patients are African American, and 62% of patients are aged 18–44 years.

The study protocol was approved by the Joint Committee on Clinical Investigation of the Johns Hopkins University School of Medicine. Patients aged 18–44 years who presented to the Johns Hopkins Hospital Adult ED between June and November 1998 for medical treatment of any nature and gave informed consent were eligible for study recruitment. Patients were excluded from the study if they were critically ill or not competent to give consent. Patients were sampled from 10:00 A.M. to 2:00 A.M., to maximize resource utilization and patient capture, as these are peak patient flow times. Sampling occurred in 10–12 8-h blocks 7 days per week. Data collection shifts were randomized to give even representation of days of the week and time of day.

ED medical records of the study participants were reviewed to determine whether the patient had been screened for STD risk by history or physical examination or if standard diagnostic laboratory assays for chlamydial or gonococcal infections had been ordered. Screening for STD risk by history was defined as documentation of at least 1 of the following: history of STD or PID, sexual activity, condom use, or information about sex-

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**Table 1. Characteristics of patients attending the Johns Hopkins Hospital Adult Emergency Department who were approached about participation in a study of the clinical aspects of the diagnosis of chlamydial infection and gonorrhea in an acute care setting.**

Characteristic	Patients enrolled in study (n = 700)	Patients who refused to be enrolled in study (n = 281)	P
Age, mean y	28.4	31.4	<.001
Age 18–31 y, %	65	49	<.001
African American, <sup>a</sup> %	88	80	.008
Males, %	42	42	.996
Median triage level	3.0	3.0	.643
Treated for chlamydial infection or gonorrhea at initial visit, %	8.9	1.5	.001

<sup>a</sup> Reference category included white, Asian, and Hispanic.

ual partners. Screening for STDs by physical examination was defined as documented examination of male genitalia or female pelvic examination (bimanually and/or with use of a speculum). We determined whether laboratory tests for chlamydial and gonococcal infections were ordered by reviewing the electronic laboratory records. Urine samples for ligase chain reaction (LCR) testing (Abbott Laboratories) were collected after survey administration. Study assessment and testing were performed independently of the clinicians' assessment in the ED. If an ED urine specimen was obtained, the same specimen was tested by LCR assay. All urine specimens were obtained at the time of ED presentation and before any treatment.

Statistical analyses were performed by using SPSS version 7.5 (SPSS) for Windows (Microsoft). Cases were defined as patients positive for *Neisseria gonorrhoeae* or *C. trachomatis* by urine LCR analysis. Infections "recognized" by clinicians in the ED were defined as STD diagnoses recorded in the medical record or treatments that are exclusively used for STDs (e.g., combination of 500 mg of ciprofloxacin or 125 mg of ceftriaxone and 1 g of azithromycin for chlamydial and gonococcal infections or a single dose of 2 g of metronidazole for trichomoniasis). Associations between variables were explored by using Pearson's  $\chi^2$  and Student's *t* tests.

**Results.** A total of 981 patients were approached for study recruitment over a 14-week period; 700 (71%) consented to participate in the study. Enrolled patients were on average younger, more likely to be African American, and more likely to have been treated for chlamydial or gonococcal infections by clinicians in the ED than were patients who refused to participate in the study (table 1). Adequate urine samples for LCR testing were obtained from 655 (94%) of 700 patients.

We divided our sample into 2 age groups (18–31 and 32–44 years of age) on the basis of the median age of the study population. The prevalence of chlamydial or gonococcal infections determined by urine LCR assay was 13.6% (59 of 434

patients) in the group aged 18–31-years and 1.8% (4 of 221) in the group aged 32–44 years.

Of the 63 infected patients, only 15 (23.8%) were appropriately treated at the ED. Results of STD assessment by ED clinical staff are presented in table 2. One-third of patients aged 18–31 years were screened by ED clinicians for STDs or STD risk by history. Male and female patients did not significantly differ with respect to the proportion who presented with genital discharge or the proportion who were treated for chlamydial or gonococcal infections. Among patients aged 18–31 years, 31.1% underwent genital examinations. Women were significantly more likely to be screened for STD risk by history, physical examination, and laboratory assay than were men, and STD was mentioned more frequently in the assessment and plan for women. Except for men with symptoms, diagnostic laboratory testing was infrequently performed.

Standard laboratory tests for chlamydial or gonococcal infections were ordered by ED staff for 100 (14.3%) of the 700 study participants (table 2). At the time of the study, the standard tests for chlamydial and gonococcal infections were either DNA probe testing (Gen-Probe) or culture of urethral or cervical specimens. Of the 100 patients who underwent testing at the ED, 97 were also tested by urine LCR analysis (table 3). Of these 97 patients, 90 were tested by DNA probe analysis for *N. gonorrhoeae*, 7 were tested by culture for *N. gonorrhoeae*, 88 were tested by DNA probe analysis for *C. trachomatis*, and 1 was tested by culture for *C. trachomatis*, all of which were mutually exclusive. Among patients who had both urine LCR and standard ED diagnostic assays, LCR detected 8 patients infected with *C. trachomatis*, 9 patients infected with *N. gonorrhoeae*, and 3 patients infected with both *C. trachomatis* and *N. gonorrhoeae*. The ED laboratory assessment detected 8 of these 20 LCR assay-positive specimens (*C. trachomatis*, 5; *N. gonorrhoeae*, 3). For 2 specimens, DNA probe test results performed at the ED were positive for *C. trachomatis* and *N. gon-*

**Table 2. Indicators of clinician suspicion for sexually transmitted disease (STD) by study subpopulation in a study of the clinical aspects of the diagnosis of chlamydial infection and gonorrhea in an acute care setting.**

Variable	Total (N = 700)	Age group		P	Sex		P
		18–31 y (n = 454)	32–44 y (n = 246)		Female (n = 403)	Male (n = 297)	
Screened for STD							
By history (n = 607)	29.5	33.3	21.5	.011	39	16	<.001
By physical examination (n = 606)	27.4	31.1	19.5	.014	38	13	<.001
Laboratory tests ordered by ED	14.3	18.9	5.7	<.001	23.6	1.7	<.001
STD noted in assessment and plan (n = 607)	14.8	15.3	13.8	.224	18	10	.005
Treated for chlamydial infection or gonorrhea (n = 673)	8.9	10.0	6.8	.319	9.4	8.3	.647
Age, mean y	28.6	24.1	37.1	<.001	27.8	29.9	<.001
Vaginal or penile discharge (n = 672)	4.8	5.9	2.6	.183	5.2	4.2	.542

**NOTE.** Unless stated otherwise, data are percents of patients with variable. ED, emergency department.

*orrhoeae* (1 each), but urine LCR analysis was negative. Therefore, compared with the sensitivity and specificity of LCR analysis, the sensitivity and specificity of ED laboratory assays were 40% and 97.4%, respectively.

The ED presumptively treated 44 (10%) of 438 patients aged 18–31 years who were enrolled in the study and 16 (6.8%) of 235 patients aged 32–44 years ( $P = .139$ ). A total of 37% of patients who received antibiotic therapy complained of genital discharge (table 4). Treatment data were missing for 27 patients (3.9%). The proportion of patients offered syndromic treatment did not differ in terms of gender.

Treated patients for whom LCR assay results were positive were similar to untreated patients for whom LCR assay results were positive with respect to age and sex (table 4). Fifty-three percent of the 15 treated patients for whom LCR assay results were positive reported genital discharge as the presenting complaint. Four (11%) of 36 women for whom LCR assay results were positive reported vaginal discharge at triage, compared with 5 (19%) of 26 men who complained of urethral discharge at triage (triage data were missing for 1 female for whom LCR analysis was positive;  $P = .370$ , Pearson  $\chi^2$ ). Of the 48 untreated

patients for whom LCR assay results were positive, 19 (40%) were male and 29 (60%) were female. Of the 48 patients with untreated infections, a total of 17 (35%) underwent screening for STDs. Of these 17 patients, 15 were screened by history, 16 were screened by physical examination, and 13 were screened by diagnostic laboratory assay ordered by the ED clinician; results of 5 diagnostic laboratory assays were positive.

Forty-five patients for whom urine LCR assay results were negative also were treated at the ED for chlamydial or gonococcal infections (table 4). Thirty-one percent of these patients reported genital discharge as a presenting complaint. These patients did not differ with respect to sex. Overall, when compared with the diagnostic sensitivity and specificity of LCR analysis as the “gold standard,” the diagnostic sensitivity and specificity of ED clinicians were 23.8% (15 of 63 patients) and 92.6% (565 of 610), respectively. For patients aged 18–31 years, the diagnostic sensitivity and specificity of ED clinicians were 23.7% (14 of 59 patients) and 91.7% (330 of 360), respectively.

**Discussion.** Chlamydial and gonococcal infections in our ED patients were often unsuspected at the initial ED visit. Patients who received treatment were more likely than patients who did not receive treatment to report obvious signs of infections, such as vaginal or penile discharge. Only 2.1% of untreated patients for whom LCR analysis was positive reported genital discharge, while 31% of treated patients for whom LCR analysis was negative reported genital discharge. Current ED practice, largely based on syndromic evaluation, highlights the low sensitivity and specificity of vaginal discharge. Relying solely on symptomatic presentation resulted in missed diagnosis of 76% of infections in our ED.

Syndromic management of urethral discharge in men and genital ulcer disease in both men and women has high, acceptable sensitivity and specificity [14]. Syndromic management of cervical infection has had consistently low sensitivity. A prospective evaluation of several complex algorithms that

**Table 3. Sensitivity and specificity of standard diagnostic laboratory assays at an emergency department (ED) vs. urine ligase chain reaction testing for gonorrhea and chlamydial infection in a study of the clinical aspects of diagnosis of sexually transmitted diseases in an acute care setting.**

ED laboratory assay result	Urine LCR test results, no.		
	Positive	Negative	Total
Positive	8	2	10
Negative	12	75	87
Total	20	77	97

**NOTE.** Sensitivity, 40% (8 of 20); specificity, 97.4% (75 of 77). LCR, ligase chain reaction.

**Table 4. Comparison of treatment and urine ligase chain reaction (LCR) assay results in a study of the clinical aspects of diagnosis of chlamydial infection and gonorrhea among patients who presented to an emergency department.**

Variable	Age, mean y	Male, %	Vaginal or penile discharge
AT given ( <i>n</i> = 60)	26.7	40	37
AT not given ( <i>n</i> = 613)	28.8	43	1.7
<i>P</i>	.035	.650	<.001
AT given, LCR <sup>+</sup> ( <i>n</i> = 15)	22.7	47	53
AT not given, LCR <sup>+</sup> ( <i>n</i> = 48)	23.9	40	2.1
<i>P</i>	.425	.633	<.001
AT given, LCR <sup>-</sup> ( <i>n</i> = 45)	28	38	31
AT not given, LCR <sup>-</sup> ( <i>n</i> = 522)	28.9	42	1.8
<i>P</i>	.218	.569	<.001

**NOTE.** AT, appropriate treatment for gonorrhea or chlamydial infection at the initial visit to the emergency department; +, positive; -, negative.

evaluate combinations of signs, symptoms, and behavioral risks for management of female attendees of an STD clinic in Seattle demonstrated sensitivities for cervical infection ranging from 50% to 87% and positive predictive values ranging from 33% to 51% [15]. For populations among which prevalences are lower, the positive predictive value of these algorithms would be further compromised.

Traditional laboratory assays for chlamydial and gonococcal infections (such as culture or DNA probe testing) make use of urethral or cervical specimens, which require urethral swabbing for men and pelvic examinations for women. The sensitivities of culture and DNA probe testing for chlamydial infection compared with a DNA amplification standard are 70%–85% and 77%–93%, respectively [16]. We found lower sensitivities when culture and DNA probe testing results were compared with urine LCR assay results. This finding may have been due to variations in health care provider technique for obtaining specimens or the lack of use of an expanded standard as the gold standard.

For the 48 untreated patients for whom LCR assay results were positive, there was a high index of clinical suspicion, as evidenced by the high proportion of patients who were screened for STD risk by history and physical examination. Many of the female patients with unrecognized infection had symptoms suggestive of genitourinary or reproductive tract infection. These data suggest that in areas where STDs are highly prevalent, clinicians may need to establish screening criteria in an ED setting or even consider presumptive treatment strategies.

There were limitations to our study that may have led to potential conservative biases in our analysis. Although the study assessment and clinical assessment were performed independently, the clinicians were not blinded to study enrollment, and some could have been aware that patients would be tested and

followed up by the study if they were positive. Health care providers may have been more likely to order laboratory tests or give treatment if they knew that their patient's outcome and disposition would be reviewed and followed up. Therefore, our data overestimate test ordering in this setting. However, with 176 different house staff rotating through the ED, some for as little as 2 weeks, the study was not a major focus of attention, and many house staff and attending clinicians were not particularly aware of the sampling periods. In addition, there may have been a volunteer bias, since the level of clinical suspicion of STD was much lower for patients who refused study participation. Those patients at higher risk of infection may have been more likely to participate in the study, leading to higher rates of detection by clinicians.

Preventing further transmission and development of sequelae of STDs is dependent on early detection [17]. The high prevalence of chlamydial and gonococcal infections among patients in this ED highlights the need for intensified STD screening, even for those patients for whom there may be a low index of clinical suspicion. In this study, detection of patients with a low index of clinical suspicion was facilitated by the use of urine LCR analysis, a noninvasive assay with proven high sensitivity and specificity. In this population, urine LCR testing was well received. From a practical standpoint, the sensitivity and specificity of LCR analysis are independent of health care provider technique. Considering the high prevalence of infection in this ED and the low sensitivity of detection based on clinical presentation, population-based screening with use of noninvasive urine testing is likely to be an effective public health intervention.

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