

The prevalence of causative organisms of community-acquired urethritis in an age group at high risk for sexually transmitted infections in Korean Soldiers

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ABSTRACT

Objectives This study was designed to evaluate the causative organisms in young male soldiers with clinical signs and symptoms after sexual contact that suggests a diagnosis of urethritis.

Methods Between June 2012 and January 2015, male patients with urethritis symptoms that had resulted from sexual contact within 3 months participated in this study. All patients were evaluated using urinalysis and were screened for *Neisseria gonorrhoeae* (NG), *Chlamydia trachomatis* (CT), *Ureaplasma urealyticum* (UU), *Mycoplasma genitalium* (MG), *Mycoplasma hominis* (MH), herpes simplex virus (HSV) type II and *Trichomonas vaginalis* (TV) using multiplex PCR (mPCR) assay in order to detect sexually transmitted infections (STI) or pathogens.

Results A total of 436 male patients aged 18–28 years were included in the study. The median age was 22.0 years. The prevalence of STI pathogens were as follows: NG in 19.0%, CT in 36.6%, UU in 24.0%, MG in 21.5%, MH in 6.1%, HSV type II in 1.6%, TV in 0.2% and indeterminate STI pathogens in 9.4%. Coinfection of NG with non-NG was detected in 5.7% of the participants, while the coinfection rates for STI pathogens were: with CT in 3.4%, with UU in 2.7%, with MG in 0.2% and with MH in 0.2%.

Conclusions CT was the most prevalent STI pathogen and coinfections of NG with non-NG appeared less frequently. The young male soldiers with urethritis should be administered suitable antibiotics for STI pathogens that were found by mPCR results, rather than an experimental combination of antibiotics for coinfections.

INTRODUCTION

Sexually transmitted infections (STI) are one of the most serious health diseases worldwide.¹ Young adults between the ages of 18 and 28 years are at high risk for STI.² Extensive global records indicate that the most common presentation of an STI is urethritis,³ which is characterised by an inflammation of the urethra, and frequently caused by sexual contact. This study was designed to evaluate the causative organisms in young male soldiers with clinical signs and symptoms after sexual contact. The result of our study suggests that it is necessary to conduct a test for urethritis for the soldiers between the age of 18 and 28 years in the South Korean armed forces. Because of its speed and preciseness, the multiplex PCR (mPCR) method was used in our research for direct identification of the

Key messages

- ▶ This study is the first investigation to evaluate the prevalence of causative organisms of urethritis in an age group that is at high risk for sexually transmitted infections.
- ▶ *Chlamydia trachomatis* (CT) was the most prevalent sexually transmitted pathogens in young male soldiers.
- ▶ The prevalence rate of coinfections of *Neisseria gonorrhoeae* with CT was 3.4%.
- ▶ Multiplex PCR assay enables direct identification of causative organisms within 1 day, with a high sensitivity and specificity.
- ▶ Suitable antibiotics should be prescribed for sexually transmitted pathogens in patients with urethritis rather than an experimental combination of antibiotics for coinfections.

causative organisms within 1 day.^{4,5} To our knowledge, our study is the first investigation to target an age group at high risk for STI to evaluate the prevalence of causative organisms of community-acquired urethritis.

METHODS

Study design and participants

A retrospective review of 14 932 young male soldiers between the ages of 18 and 28 years who visited the Armed Forces Capital Hospital from June 2012 to January 2015 for urologic disease was conducted. Among the 706 patients diagnosed with an STI, urethritis accounted for 436 (2.9% of the total number of presentations), syphilis 123 (0.8%) and penile condyloma 157 (1.0%). The 436 patients who were diagnosed with urethritis following sexual contact within 3 months were enrolled in our study. All the patients showed urethritis symptoms, including urethral discharge and/or dysuria. Patients with multiple sexual partners were defined as patients who had more than two active sexual partners within 3 months from the day the survey was conducted. Approval for the study was obtained from the institutional review board (IRB) at our hospital. Written informed consent was not required for our study according to the IRB, as the possible violation of patient rights was considered to be negligible.



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Sample collection

Urethral samples were collected from 436 patients by inserting cotton swabs 2–4 cm into the urethra and rotating them for 3–5 s. Before the insertion, the external urethral meatus was cleaned with sterile cotton swabs. Patients were instructed not to urinate for at least 1 h prior to specimen collection; the first 10–60 mL of voided urine from each patient was collected in a sterile plastic, preservative-free collection cup as a urine specimen.

Laboratory processing for organisms of community-acquired urethritis

After being maintained at room temperature, the urethral swabs were centrifuged at 5000 ×g for 15 min. The floaters were filtered, and the smaller particles were resuspended in 1 mL 1× PBS before the DNA was obtained. Genomic DNA was obtained from the pretreated urethral swab samples, and a Greencross Medical Science detection kit was used to perform mPCR amplification with a high retention of genetic sequences for the seven chosen organisms. The mPCR kit is a validated testing kit with 96% sensitivity and 98% specificity. It is validated for *Neisseria gonorrhoeae* (NG), *Chlamydia trachomatis* (CT), *Ureaplasma urealyticum* (UU), *Mycoplasma genitalium* (MG), *Mycoplasma hominis* (MH), herpes simplex virus (HSV) type II and *Trichomonas vaginalis* (TV). After separating the amplified mPCR products and identifying them by electrophoresis, the samples were moved onto a chip, and its DNA sequences were identified. Greencross Medical Science software was used to analyse each sample and detect the particles that yielded a positive result. The results of the presented matching matrix were used to identify the different types of pathogens. The mPCR kit used in our study did not differentiate between UU and *Ureaplasma parvum*. Urine samples were maintained at room temperature and transported to the laboratory medicine department at our hospital within 1 day for urinalysis.

Statistical analysis

Statistical Package for the Social Sciences (SPSS) V18.0 (SPSS Inc, Chicago, Illinois, USA) was used for all statistical analyses. The prevalence estimates of STI pathogens were calculated as the number of positive responses on mPCR.

RESULTS

This study included 436 male patients from ages of 18 to 28 years with a median age of 22.0 years. All the participants had a history of sexual contact within 3 months, with 352 (80.7%) having had multiple sexual partners. Urethral discharge was reported by 386 patients (88.5%) and dysuria by 343 patients (78.6%). All the patients reported at least one urethral discharge and/or dysuria and 231 (52.9%) were found to have pyuria (at least five white blood cells per high-power field) on laboratory testing (Table 1). The prevalence of STI pathogens is

Table 1 Patient characteristics

No. of patients	436
Median age (years)	22.0 (range, 18–28)
Sexual contact history	436 (100%)
Multiple sex partner	352 (80.7%)
Urethral discharge	386 (88.5%)
Dysuria	343 (78.6%)
Pyuria	231 (52.9%)

Table 2 The overall prevalence of sexually transmitted pathogens

Sexually transmitted pathogens	Number (%)
<i>Neisseria gonorrhoeae</i>	83 (19.0)
<i>Chlamydia trachomatis</i>	160 (36.6)
<i>Ureaplasma urealyticum</i>	105 (24.0)
<i>Mycoplasma genitalium</i>	94 (21.5)
<i>Mycoplasma hominis</i>	27 (6.1)
Herpes simplex virus type II	7 (1.6)
<i>Trichomonas vaginalis</i>	1 (0.2)
Indeterminate pathogens	41 (9.4)

given in Table 2; coinfection of NG with non-NG was detected in 25 participants (5.7%) (Table 3) and multiple coinfections in 51 (11.6%) patients (Table 4).

DISCUSSION

CT is the most prevalent causative organism for urethritis, accounting for 30–40% of the cases⁶ and made up the largest portion (36.6%) of STI pathogens in the male soldiers in our study. While previous studies have mostly been conducted in asymptomatic patients,^{7–9} this study confirmed that CT is the most prevalent causative organism in symptomatic patients as well.

Gonorrhoea is caused by the Gram-negative diplococcus NG; single exposure can increase the risk of infection for 10% in men and 40% in women.² After infection, males, in particular, will experience dysuria with mucopurulent urethral discharge. According to a study of 2672 sexually active adolescents, asymptomatic gonorrhoea accounted for 1.9% of the infections among males.¹⁰ In this study, symptomatic gonorrhoea made up 19.0% of cases of STI pathogens.

UU has been recognised as a causative organism for urethritis since the 1950s, but is often isolated in healthy male adults, and no significant difference has been reported in the prevalence between men with and without urethritis,¹¹ but some reports have indicated that UU is a causative organism for chronic urethritis.¹² This data identify UU as being present in 24.0% of patients with STI showing that UU should be considered as causative organism for urethritis.

MG is responsible for a significant number of persistent and/or recurrent cases of urethritis and based on Manhart's report, failed clinical treatments for urethritis mostly occurs in the presence of MG;¹³ it is the causative organism for persistent or recurrent urethritis in 13–41% of cases,^{14 15} which is comparable to the 21.5% of patients with MG infection in this study. MH is also frequently detected in the urethra but is not generally recognised as a pathogen in healthy men, although it can be

Table 3 The prevalence of coinfection of NG with non-NG STP identified by mPCR

Sexually transmitted pathogens	Number (%)
NG with <i>Chlamydia trachomatis</i>	15 (3.4)
NG with <i>Ureaplasma urealyticum</i>	12 (2.7)
NG with <i>Mycoplasma genitalium</i>	1 (0.2)
NG with <i>Mycoplasma hominis</i>	1 (0.2)
Total	25 (5.7)

mPCR, multiplex PCR; NG, *Neisseria gonorrhoeae*; STP, sexually transmitted pathogen.

Table 4 The prevalence of coinfection by various non- NG STP identified by mPCR

Sexually transmitted pathogens	Number (%)
CT with UU	24 (5.5)
CT with MG	8 (1.8)
CT with MH	5 (1.1)
CT with HSV type II	1 (0.2)
UU with MG	15 (3.4)
UU with MH	4 (0.9)
Total	51 (11.6)

CT, *Chlamydia trachomatis*; HSV, Herpes simplex virus type II; MG, *Mycoplasma genitalium*; MH, *Mycoplasma hominis*; mPCR, multiplex PCR; NG, *Neisseria gonorrhoeae*; STP, sexually transmitted pathogen; UU, *Ureaplasma urealyticum*.

pathogenic in patients with leukaemia.¹⁶ Kilic *et al*¹⁷ reported that the prevalence of MH was 4–13%. The prevalence of MH in patients with STI was 6.1%, and it did cause clinical signs and symptoms of urethritis in our study, and so MH should be considered a potential causative organism in young male patients who present with clinical signs and symptoms of urethritis.

The localisation of herpetic lesions in the urethra has been recognised since the end of the 19th century.² The disease generally becomes apparent after normal or buccal sexual contact.² The appearance of secretions is similar to that of non-bacterial urethritis: mucus, a few epithelial cells, a few pus globules and scanty extracellular microorganisms.¹⁸ In this study, HSV type II was observed in seven patients, all of whom had genital ulcers and a history of oral sex. TV, which is caused by a flagellated protozoan, is one of the most common STIs, with approximately 174 million new cases reported worldwide each year;¹⁹ this study included only one patient with TV, suggesting the prevalence of TV is relatively low in young male soldiers. On the other hand, pathogens in 9.4% of patients in our study could not be identified. This indeterminate figure could result from different factors, including spontaneous resolution of STI pathogens and/or presence of newly discovered pathogens, such as *Neisseria meningitidis*.²⁰

According to the literature, patients with NG are often coinfecting with CT.² It has been recommended that patients undergo simultaneous dual treatment because the cost of this type of treatment is less than that of chlamydial testing.² However, our study indicated that the prevalence rate of coinfections of NG with CT was only 3.4%. In addition, the total number of coinfections of NG with non-NG was as low as 5.7%. The mPCR method enables direct identification of causative organisms within 1 day, with a high sensitivity and specificity.^{4, 5}

This study has some potential limitations. First, owing to the retrospective nature of the study, the results of testing and treatment of our patients' sexual partners was not fully acquired. A prospectively designed study with standardised protocols that evaluates the sexual partner's pathogens and the result of treatment is needed in the near future. Moreover, the subjects of our cohort study were collected from a single institution, thus further studies to evaluate the prevalence of STI in all army recruits (with or without urethral symptoms) and to compare that with a matched group of men in Korea are expected in the near future.

Conclusion

For the efficient and effective diagnosis of urethritis in young male soldiers, we suggest that mPCR should be conducted in advance; suitable antibiotics should be prescribed for STI pathogens in patients with urethritis rather than an experimental combination of antibiotics for coinfections.

Collaborators WonKuk Cho (student of Washington University in St Louis) offered excellent English editing, A Ram Doo (clinical professor of Chonbuk National University Hospital) offered advice on content and style.

Contributors All authors contributed to authorship of the article. HJK and JKP contributed equally to this study. YSS is responsible for the overall contents.

Competing interests None declared.

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