

# Epidemiological Trends of Sexually Transmitted Infections Among Women in Cheonan, South Korea, 2011–2017

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Sexually transmitted infections (STIs) are a global health concern and can cause serious complications such as miscarriage, premature birth, and pelvic infection in pregnant women. Therefore, accurate diagnosis and information on the epidemiologic trends are critical. However, studies of STI trends in Cheonan, South Korea, have not been conducted since 2012. We examined the STI trends in the Cheonan area after 2012. From January 2011 to September 2017, 3,362 cervical swab specimens from female patients were sampled at the Dankook University Hospital and analyzed by multiplex PCR. Of the 3,362 specimens, 1,281 were positive for pathogens (38.92%). A total of 1,893 pathogens were detected. *Ureaplasma urealyticum*, *Mycoplasma hominis*, and *Chlamydia trachomatis* were the most frequent pathogens, accounting for 36.29% (687/1,893), 30.16% (571/1,893), and 19.97% (378/1,893) of the pathogen-positive samples, respectively. In the 2009–2012 analysis, *M. hominis* was identified as the predominant pathogen in STI samples, whereas *U. urealyticum* was identified as the major pathogen in this study. In many countries, including South Korea and the United States, the rate of STIs is increasing, while a decreasing trend was observed in Cheonan.

**Keywords:** Sexually transmitted infection, *Ureaplasma urealyticum*, *Mycoplasma hominis*, STI incidence, Cheonan, Korea

## Introduction

Sexually transmitted infections (STIs) spread through sexual contact and have a profound impact on sexual and reproductive health worldwide [1]. Accurate diagnosis of STIs is critical because they can cause serious complications such as miscarriage, premature birth, and pelvic infections in pregnant women [1–3].

The causative pathogens of STIs include bacteria, viruses, protozoa, and fungi. The major causative pathogens are *Ureaplasma urealyticum* (UU), *Mycoplasma*

*hominis* (MH), *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG), *Mycoplasma genitalium* (MG), and *Trichomonas vaginalis* (TV) [3].

UU and MH are frequently found in the commensal flora of the lower genital tract [4–6]. Until the 1970s, UU was considered a non-pathogenic bacterium normally present in the genitourinary tract [5]. However, recent studies have linked UU and MH with maternal complications such as miscarriage, pelvic inflammation, and premature labor in pregnant women. Infection with these organisms during pregnancy can also cause respiratory disease and sepsis in newborns [5, 7].

CT is a major cause of non-gonococcal chlamydial infection [8]. CT infection in the genital tract can cause pelvic inflammation, extra uterine pregnancy, chronic pelvic pain, and epididymitis [8, 9]. Furthermore, CT

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infection during pregnancy can cause neonatal conjunctivitis and pneumonia [10].

NG is the etiologic agent of gonorrhoea, which typically manifests as a mucosal infection of the lower genital tract of women [11]. Gonorrhoea has the highest probability of transmission per sexual contact [12].

MG, which is a *Mycoplasma* spp. like UU and MH, is a major cause of unstable urethritis and may cause complications in pregnant women and neonatal infection [13, 14]. There is also increasing evidence that MG causes mucopurulent cervicitis in women [15].

The World Health Organization estimates that 1 million new cases of STIs are reported every day, and the Centers for Disease Control and Prevention (USA) estimates that there are 20 million new cases of STI in the United States each year [1, 16]. Because of the high incidence rates and global prevalence, STI trends have been studied worldwide. However, the STI trends in Cheonan have not been studied since 2012. Thus, we examined the STI trends in the Cheonan area after 2012.

We determined the female STI trend in the Cheonan area by analyzing the results of a 7-year STI screening of female patients who visited the Dankook University Hospital. Furthermore, we compared the trends in pathogen species, patient age, and infection season, as well as the frequency of single and multiple infections, with those reported by the study of STI detection trends in Cheonan from 2006 to 2012 [17].

## Materials and Methods

### Materials

From January 2011 to September 2017, 3,362 cervical swab specimens were collected from women who had undergone screening for STI at the Dankook University Hospital (Cheonan, Korea). This study was approved by

the Dankook University Institutional Review Board (IRB file No. 2017-10-004).

### Methods

**DNA extraction.** The collected clinical specimens were stored at  $-70^{\circ}\text{C}$  until isolation of DNA for multiplex PCR (mPCR). The swab specimen was suspended in phosphate buffered saline (PBS) and collected by centrifugation at  $13,000 \times g$  for 10 min. The supernatant was discarded and the pellet was resuspended in PBS. DNA for the mPCR assay was extracted using a QIAamp DNA Mini Kit (Qiagen, Germany) in accordance with the manufacturer's instructions. Approximately 200  $\mu\text{l}$  of each specimen was used as starting material for DNA isolation. Concentrations of the extracted DNA samples were measured using NanoDrop 1000 (Thermo Fisher Scientific, USA).

**Multiplex PCR.** The mPCRs for the STIs were performed using the Seeplex STD Detection Kit (Seegene, Korea) according to the manufacturer's instructions using a PTC 200 PCR system (MJ Research, USA). Briefly, 5  $\mu\text{l}$  of extracted DNA was added to the PCR tube from the Seeplex STD Detection Kit containing 5  $\mu\text{l}$  of a primer and probe mixture and 10  $\mu\text{l}$  of mPCR premix for the six STI pathogens UU, MH, CT, NG, MG, and TV. Detection of these six pathogens was performed simultaneously in a single mPCR using a combination of primers for each pathogen. The target genes and their sizes for the six types of STIs are listed in Table 1. The initial PCR step was performed at  $94^{\circ}\text{C}$  for 15 min, followed by 40 cycles under the following conditions:  $94^{\circ}\text{C}$  for 30 s,  $63^{\circ}\text{C}$  for 90 s, and  $72^{\circ}\text{C}$  for 90 s. The final cycle was followed by an extension step at  $72^{\circ}\text{C}$  for 10 min to complete partial polymerization. Positive and negative PCR controls containing standardized viral RNA

**Table 1. Detection targets of mPCR assays for various pathogens involved in sexually transmitted infections.**

	Target	Gene	Size (bp)
<i>Arabidopsis</i> (internal control)	<i>CESA3 719</i>		719
<i>Trichomonas vaginalis</i>	<i>Actin</i>	<i>L05468</i>	580
<i>Mycoplasma hominis</i>	<i>Gap</i>	<i>Aj243692</i>	502
<i>Ureaplasma urealyticum</i>	<i>Urease</i>	<i>AF085729</i>	435
<i>Chlamydia trachomatis</i>	<i>Cryptic plasmid</i>	<i>M19487</i>	348
<i>Mycoplasma genitalium</i>	<i>gyrA</i>	<i>L43967</i>	253
<i>Neisseria gonorrhoeae</i>	<i>Por A pseudogene</i>	<i>AJ223447</i>	214

**Table 2. Percentage of various pathogens detected in sexually transmitted infection-positive samples.**

Pathogen	Number (%)
<i>Ureaplasma urealyticum</i> (UU)	687 (36.29)
<i>Mycoplasma hominis</i> (MH)	571 (30.16)
<i>Chlamydia trachomatis</i> (CT)	378 (19.97)
<i>Neisseria gonorrhoeae</i> (NG)	100 (5.28)
<i>Mycoplasma genitalium</i> (MG)	80 (4.23)
<i>Trichomonas vaginalis</i> (TV)	77 (4.07)
Total	1,893 (100)

extracts and nuclease-free water, respectively, were included in each run. The kit includes reagents for amplifying the *Arabidopsis* cellulose synthase (*CESA3*) gene as an internal control (IC), which is designed to detect the presence of PCR inhibitors. An IC was included in the PCR mixture to detect the presence of PCR inhibitors. PCR products were separated by ethidium bromide-stained 2% agarose gel electrophoresis and visualized under ultraviolet light.

### Statistics

Patient characteristics at the time of admission, including detected pathogen, age, and season, were ana-

lyzed retrospectively. A p-value < 0.05 was considered significant.

## Results

A total of 3,362 specimens were collected from 3,014 women. Of these, 1,281 specimens (38.92%) tested positive and 1,893 pathogens were detected. Of the 1,893 pathogens detected, 36.29% were UU, 30.16% were MH, and 19.97% were CT (Table 2).

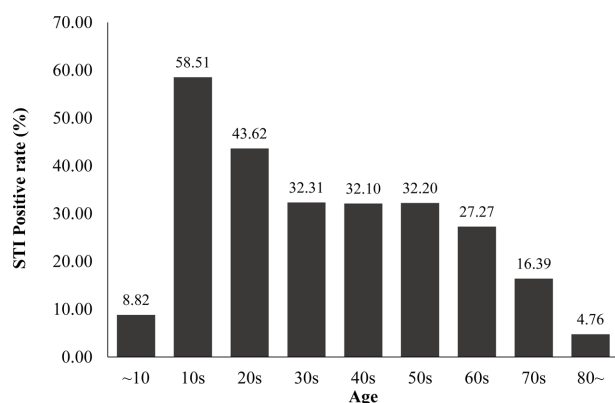
Of the 1,281 positive specimens, 65.34% (837/1,281) and 34.66% (444/1,281) specimens tested positive for single and multiple pathogens, respectively. Of the specimens with multiple infections, 23.5% (301/1,281) were double infections and 9.45% (121/1,281) were triple infections.

Among the samples with a single infection, the UU infection rate was the highest (41.22%, 345/837), MH was the second highest (31.78%, 266/837), and CT was the third highest (19.59%, 164/837). Among the double infections, co-infection of UU and MH was the most common (46.84%, 141/301), followed by UU and CT co-infections (14.95%, 45/301), and MH and CT co-infections (11.96%, 36/301) (Table 3).

**Table 3. Frequency of single-, double-, and multiple-positive infections based on multiplex PCR assays.**

Single-positive infection	No. (%)	Double-positive infection	No. (%)	Triple-positive infection	No. (%)		
UU	302 (40.21)	UU	MH	141 (46.84)	UU & MH	CT	43 (35.54)
MH	246 (32.76)		CT	45 (14.95)		TV	13 (10.74)
CT	148 (19.71)		NG	13 (4.32)		NG	8 (6.61)
TV	24 (3.2)		MG	12 (3.99)		MG	6 (4.96)
MG	17 (2.26)		TV	7 (2.33)	UU & CT	NG	24 (19.83)
NG	14 (1.86)	MH	CT	36 (11.96)		MG	6 (4.96)
			TV	18 (5.96)		TV	2 (1.65)
			MG	7 (2.33)	UU & TV	NG	1 (0.83)
			NG	1 (0.33)	MH & CT	MG	5 (4.13)
		CT	NG	13 (4.32)		TV	3 (2.48)
			MG	5 (1.66)		NG	3 (2.48)
			TV	1 (0.33)	MH & TV	NG	1 (0.83)
		NG	TV	1 (0.33)	CT & MG	NG	3 (2.48)
		MG	NG	1 (0.33)	CT & TV	MG	2 (1.65)
					NG	1 (0.83)	
Total	751 (100)			301 (100)			121 (100)

UU: *Ureaplasma urealyticum*; MH: *Mycoplasma hominis*; CT: *Chlamydia trachomatis*; TV: *Trichomonas vaginalis*; MG: *Mycoplasma genitalium*; NG: *Neisseria gonorrhoeae*.

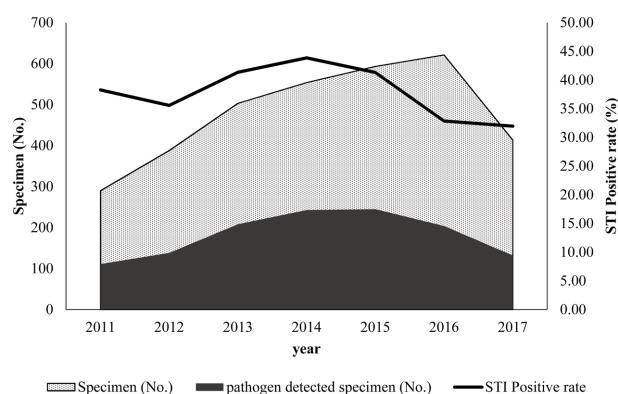


**Fig. 1. STI-positive rate by age.**

The mean age of the positive women was 31.9 years (mid-age 29.0 years, range 0.0–92.1). The average age of TV-, MH-, and UU-positive patients was 37.1, 32.7, and 31.4 years, respectively. The mean age of patients with single and double infections was 33.99 and 30.8 years, respectively. The average age of patients with triple infections was 26.75 years. The average age (years) of patients testing positive for infection was 33.55 in 2011, 33.5 in 2015, and 32.20 in 2013 (Fig. 1). Infections were most prevalent among individuals aged 10–20 years (58.51%, 282/482), followed by those aged 20–30 years (43.62%, 383/878). In terms of age, the UU infection rate was highest and MH was second highest for all age groups, except for patients in their 40 s, 70 s, and 80 s.

## Discussion

Compared to STD data from women in Cheonan obtained from 2006 to 2012, the present findings indicate an increased detection of UU. In the previous study, MH accounted for 62.1% of the six pathogens detected [17]. However, among the 1,893 pathogens detected in this study, UU was detected most frequently at a rate of 36.29% followed by MH with 30.16%. The detection rate of UU was the highest at 40.21% (302/751), even in samples displaying an infection by one pathogen. Although the rate of detection of multiple infections was high, 72.43% of double infections including UU were the most common, and triple infections were the highest (85.12%). This is similar to the results of previous studies, where UU was detected in 54.5% (18/33) of single infections and 74.41% (10/14) of multiple infections [18], and the



**Fig. 2. Annual incidence of sexually transmitted infections and number of specimens.**

detection rate of *Ureaplasma* spp. was 54.96% (493/897) [19].

The annual STI rate was the highest at 43.55% (243/554) in 2014. Thus, STI incidence showed a decrease every year (Fig. 2). *Ureaplasma* spp. can be divided into UU and *U. parvum*. Recently, there is a need to detect these two bacteria separately. UU is the most common STD strain in Korean women [20]. In some cases, pregnant women are infected with UU, which can lead to miscarriage, premature labor, and low birth weight [5, 7, 20]. Hence, the detection of *Ureaplasma* spp. is important.

The average age of the female subjects was 35.1 years and the mean age was 31.9 years. The median age was 29.0 years (range 0.0–92.1 years). The mean age of patients with multiple mycobacterial infections was 29.2 years, compared with a mean age of 33.99 years for those with an infection caused by one pathogen. Among those with multiple infections, the mean age of the double- and triple-infected patients was 30.8 and 26.75 years, respectively. The greater the number of coinfecting pathogens, the lower was the average age.

The purpose of this study was to investigate the prevalence of STI due to UU, MH, CT, TV, MG, and NG in Cheonan women. The prevalence of annual STI in Cheonan is gradually decreasing. This result is in contrast with the increasing STI rate worldwide. This may be because of the small number of specimens in patients 10–20 years of age with a high infection rate. The number of specimens in women less than 20, 20–29, 30–39, 40–49, 50–59, and 60–69 years of age was 482, 878, 752, 729, 295, and 110, respectively. The number of speci-

mens from the youngest women was smaller than that from all age groups except the eldest women. These specimens were provided by the provincial tertiary hospitals in the Cheonan area. Additional studies are needed to examine the rates in other areas.

This study reports the trends in STD prevalence in Cheonan. The findings can be used as a reference for further clinical studies.

## Acknowledgment

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## Conflict of Interest

The authors have no financial conflicts of interest to declare.

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## 국문초록

### 2011년부터 2017년까지 천안에서의 STI 감염 양상

박지은<sup>1†</sup>, 전재식<sup>1†</sup>, 김종완<sup>2</sup>, 김재경<sup>1\*</sup>

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성병(Sexually transmitted infection, STI)은 전세계적인 건강 문제이며 임신부의 유산, 조기 출산, 골반 내 감염과 같은 심각한 합병증을 유발할 수 있다. 따라서 정확한 진단 및 역학 동향에 대한 정보가 중요하다. 그러나 2012년 이후 천안의 STI 추세에 대한 연구는 이루어지지 않았다. 이에 저자들은 2012년 이후 천안의 STI 추이를 조사했다. 2011년 1월부터 2017년 9월까지 단국대학교에 방문한 여성 환자에서 채취한 3,362개의 자궁 경부 샘플을 multiplex PCR 방법으로 분석했다. 3,362개의 표본 중 1,281개가 STI 양성이었다(38.92%) 총 1,893개의 병원균이 검출되었다. *Ureaplasma urealyticum*, *Mycoplasma hominis* 및 *Chlamydia trachomatis*가 병원체 양성 검체에서 각각 36.29% (687/1,893), 30.16% (571/1,893) 그리고 19.97% (378/1,893)를 차지하는 가장 흔한 병원균이었다. 2009-2012년 분석에서는 *M. hominis*가 가장 흔하게 검출됐지만 이번 연구에서는 *U. urealyticum*가 가장 흔하게 검출됐다. 한국과 미국을 비롯한 많은 국가에서 STD 발병률이 증가하는 반면 천안에서는 감소하는 경향이 나타났다.