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Prevalence of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections in Republic of Korea: Impacts of Sex, Age, and Testing Method

[1]Hyeok-Jin Kwon, [2]Sun-Gyu Kim, [3]Junmin Lee, [3]Dongin Seok and [1]Jae Kyung Kim

[1]Department of Biomedical Laboratory Science, Dankook University College of Health Sciences, Cheonan, Republic of Korea
[2]Department of Clinical Laboratory Science, Dongnam Health University, Suwon, Republic of Korea
[3]U2Labs, Jangwon Medical Foundation, Seoul, Republic of Korea

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Corresponding Author:
Jae Kyung Kim
Department of Biomedical Laboratory Science, Dankook University College of Health Sciences, Cheonan, Republic of Korea
Email: nerowolf2@dankook.ac.kr

Abstract: The prevalence of Sexually Transmitted Diseases (STDs) is increasing globally, necessitating a quick and accurate diagnosis method for appropriate treatment selection. An analysis of venereal diseases conducted at U2Bio (Jangwon Medical Foundation, Seoul, Republic of Korea) over a 2-year period showed that *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) infection rates were related to sex, age, and specimen type. We hypothesized that the prevalence of CT and NG varied depending on these factors and statistically analyzed STD prevalence in Korea to provide case data for future STD research. We employed multiplex PCR (mPCR) to analyze 343,071 specimens collected between January 2018 and December 2020 for 12 STD-causing pathogens. Our findings revealed that 34.7% (n = 119,232/343,071) of specimens tested positive for one or more STD-causing pathogens, with females exhibiting an overall higher positivity rate than males. Of the 119,232 positive specimens, 25.0% (n = 29,785/119,232) were CT-positive cases, 10.2% (n = 12,150/119,232) of the cases were NG-positive, and males had markedly higher CT and NG positivity rates than females, along with higher co-infection rates. The prevalence of both CT and NG infections predominated in the 20-29 age group at 49.4% (n = 14,686/29,785) and 43.6% (n = 5,296/12,150), respectively; the prevalence decreased with age, consistent with previous studies. These findings suggest that sex, age, and sampling methods are important factors that need to be considered when developing effective STD prevention and management strategies. However, our study has limitations in that a comparative analysis could not be performed with the data collected from other institutions, making it necessary to collect data from other inspection agencies other than U2Bio and to conduct a follow-up study in the future.

Keywords: Co-Infection, Sexually Transmitted Infection, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*

Introduction

The prevalence of venereal diseases, including those caused by *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG), is gradually increasing worldwide (Seo *et al*., 2021). Despite variations among countries, sexually transmitted diseases (STDs) arising from infections with CT and NG have high overall prevalence rates (Ford and Decker, 2016; Dubbink *et al*., 2018). CT is associated with various conditions such as cervical inflammation and ectopic pregnancy in females and non-gonococcal urethritis and paratesticular cancer in males (Lee *et al*., 2022). NG is the causative agent of gonococcal gonorrhea in females and its annual increased prevalence (Kim, 2013; Lee *et al*., 2022) is related to reinfection via asymptomatic infection (Hocking *et al*., 2013; Lanjouw *et al*., 2016; Chang *et al*., 2020).

STDs can lead to multiple complications; they damage reproductive tissues, cause inflammation and deformation, and are related to increased rates of infertility (Yeoh *et al*., 2020). STDs of reproductive organs are common and can be transmitted asymptomatically. Furthermore, treatment failure can occur because of recurrent reinfections via exposure to infected partners during unprotected sex (Hocking *et al*., 2013; Lanjouw *et al*., 2016).

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CT is the only human pathogen from the genus *Chlamydia*, and accurate testing for CT and NG is crucial. In this respect, nucleic acid amplification tests are recommended to identify *Chlamydia* in clinical specimens (Hocking *et al*., 2013; Curry *et al*., 2019; Leonard *et al*., 2019). In addition, appropriate specimen collection methods are vital for minimizing errors and ensuring accurate STD testing. CT and NG predominantly infect the urethra and endocervical epithelium in males and females, respectively, (Leonard *et al*., 2019), and co-infections with CT and NG are prevalent (Dubbink *et al*., 2018). Cotton swabs of the lesion site are the most sensitive and appropriate specimen collecting method (Yuk *et al*., 2021).

Co-infections with venereal disease-causing microorganisms, specifically CT and NG, are on the rise and are associated with age and sex (Seo *et al*., 2021). Among males, NG infection is related to a high risk of contracting other venereal diseases (Sedeh *et al*., 2021). Additionally, females with CT infections have a high risk of peripheral angiitis and other venereal diseases (Baeten *et al*., 2001; Wasnik *et al*., 2022). CT and NG co-infections are more strongly correlated with CT infections than with NG infections (Su *et al*., 2022). Therefore, co-infections can affect different causative agents. For example, patients infected with herpes simplex virus, the primary cause of genital ulcer disease, also show high rates of CT and NG co-infections (Mungati *et al*., 2018).

An analysis of venereal diseases conducted at U2Bio (Jangwon Medical Foundation, Seoul, Republic of Korea) over a 2-year period showed that CT and NG infection rates were related to sex, age, and specimen type. We hypothesized that the prevalence of CT and NG varied depending on these factors and statistically analyzed STD prevalence in Korea to provide case data for future STD studies. We aimed to employ real-time PCR to detect the target genes of each pathogen.

Materials and Methods

DNA Extraction

A total of 343,071 samples were collected from patients who visited the General Practitioner and Semi Hospitals in the Republic of Korea between January 2018 and December 2020 and requested molecular biological tests at U2Bio (Jangwon Medical Foundation, Seoul, Republic of Korea). The samples included urine (n = 267,386), cotton swabs (n = 14,876), affected area tissues (n = 2), and others (blood and sputum) (n = 60,807) from male (n = 291,485) and female (n = 51,586) patients ranging in age from 2–99 years. The samples were stored at -70°C until they were processed for DNA extraction using an Exi Prep TMD × Bacteria Genomic DNA Kit (Bioneer, Seoul, Republic of Korea). The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of the Clinical Research Review Committee of Dankook University (Institutional Review Board DKU, certificate no. DKU 2021-04-002).

Multiplex PCR

The AccuPower Multiplex® STI8A-Plex Real-Time PCR Kit (Bioneer, Seoul, Republic of Korea) was used to analyze the extracted DNA. Multiplex real-time PCR was performed according to the manufacturer's protocol under the following cycling conditions: 45 cycles for 5 min at 95°C, 5 s at 95°C, and 5 s at 55°C.

Pathogen Detection

Using multiplex PCR and target DNA, we identified 12 types of STD-causing pathogens in the samples: *Candida albicans*, CT, *Gardnerella vaginalis*, HSV type I, HSV type II, NG, *Mycoplasma genitalium*, *Mycoplasma hominis*, *Treponema pallidum*, *Trichomonas vaginalis*, *Ureaplasma urealyticum*, and *Ureaplasma parvum*. Among these, NG and CT were analyzed.

Results

Sex Analysis

Among the male individuals tested, 33.6% (n = 97,902/291,485) were positive for STDs. Of these, 28.4% (n = 27,831/97,902) were positive for CT and 12.1% (n = 11,826/97,902) were positive for NG. Among female individuals, 41.3% (n = 21,330/51,586) tested positive for STDs, 9.2% (n = 1,954/21,330) positive for CT, and 1.5% (n = 324/21,330) were positive for NG (Table 1) and (Figs. 1-2).

Table 1: Positive samples for *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Chlamydia trachomatis* and *Neisseria gonorrhoeae* co-infection

	Both sexes	Male	Female
Total Infection-positive samples	34.8%	33.6%	41.3%
No.	119,232	97,902	21,330
CT positivity	25.0%	28.4%	9.2%
No.	29,785	27,831	1,954
NG positivity	10.2%	12.1%	1.5%
No.	12,150	11,826	324
CT and NG positivity	1.7%	2.0%	0.4%
No.	2,050	1,965	85

STDs, Sexually Transmitted Diseases; CT, *Chlamydia trachomatis*; NG, *Neisseria gonorrhoeae*

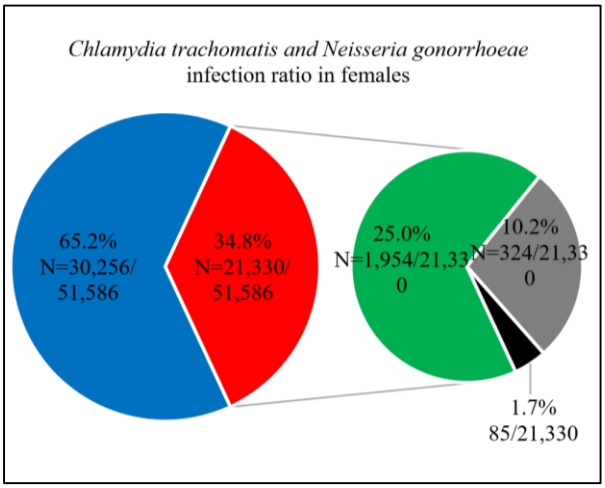

Fig. 1: The left circle represents the positivity and negativity ratios in females, while the right circle shows the STD positivity rate among CT, NG, and co-infection with both pathogens. Blue: Negative samples; red: Positive samples; green: CT-positive samples; gray: NG-positive samples; black: Samples positive for both CT and NG

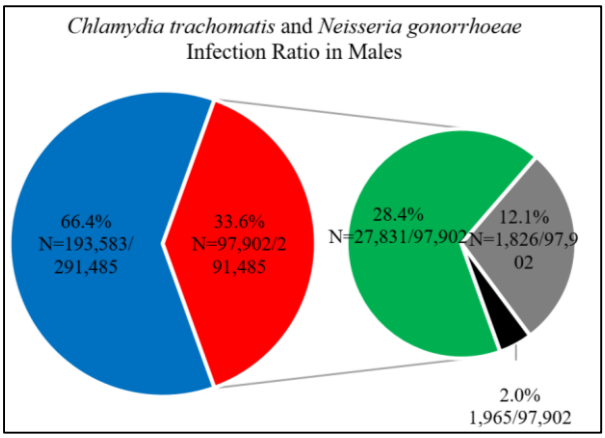

Fig. 2: The left circle represents the positivity and negativity ratios, while the right circle shows STD positivity rates among CT, NG, and co-infection with both pathogens. Blue: Negative samples; red: Positive samples; green: CT-positive samples; gray: NG-positive samples; black: Samples positive for both CT and NG

Swab collection provided the highest all-STD positivity rates: 49.0% (N = 421/859) for males and 56.3% (n = 7,894/14,017) for females. Different positivity rates were observed for each pathogen and between sexes.

The all-STD positivity rates using the urine collection method were 33.8% (n = 82,782/244,683) and 38.4% (n = 8,719/22,703) for males and females, respectively. Among the sample collection methods that showed a positivity rate for STD pathogens, urine collection showed the highest rate of 76.7% (n = 91,501/119,232), whereas the rate via swab collection was 7.0% (n = 8,315/119,232). Overall, females had a higher positivity rate than males, and swab collection showed higher positivity rates compared to urine collection (Table 2).

Co-Infection

Among CT-positive samples, the rate of CT and NG co-infection was 1.71% (n = 2,050/119,232) overall, 2.0% (n = 1,965/97,902) in males, and 0.4% (n = 85/21,330) in females (Table 3).

The positivity rate for CT infection without co-infection was 49.4% (n = 14,686/29,758) in the 20–29 age group, decreasing with age. In contrast, the positivity rate for co-infections was highest in the 20–29 age group (56.1%, n = 6,470/11,539), whereas the 70–79 age group showed the lowest rate of co-infection (0.1%, n = 9/11,539) (Table 4) and (Fig. 3).

Table 2: STD positivity rate by sex, based on sample collection method

	Both sexes (%)	No.	Male (%)	No.	Female (%)	No.
Total	34.8%	119,232	34.8%	97,902	41.3%	21,330
Urine	76.7%	91,501	33.8%	82,782	38.4%	8,719
Swab	7.0%	8,315	49.0%	421	56.3%	7,894
Others	16.3%	19,416	32.0%	14,699	31.7%	4,717

STD, sexually transmitted disease

Table 3: Ratio of *Chlamydia trachomatis* infection and *Chlamydia trachomatis* and *Neisseria gonorrhoeae* co-infection by sex

	Male (%)	No.	Female (%)	No.
CT	93.5	27,831	6.5	1,927
CT and NG	7.0	1,965	4.4	85

CT, *Chlamydia trachomatis*; NG, *Neisseria gonorrhoeae*

Table 4: Ratio of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections as well as *Chlamydia trachomatis* and *Neisseria gonorrhoeae* co-infection by age, as determined using mPCR detection assay

Age group (years)	CT	No.	NG	No.	CT and NG	No.
(≥19)	4.5%	1,339	7.6%	927	12.6%	259
(20–29)	49.4%	14,686	43.6%	5,296	49.8%	1,020
(30–39)	27.6%	8,212	29.9%	3,628	25.6%	524
(40–49)	12.8%	3,818	13.3%	1,614	9.2%	189
(50–59)	4.7%	1,399	4.5%	551	2.5%	52
(60–69)	0.9%	270	1.0%	116	0.2%	4
(≤70)	0.1%	31	0.1%	17	0.1%	2

CT, *Chlamydia trachomatis*; NG, *Neisseria gonorrhoeae*; mPCR, Multiplex polymerase chain reaction

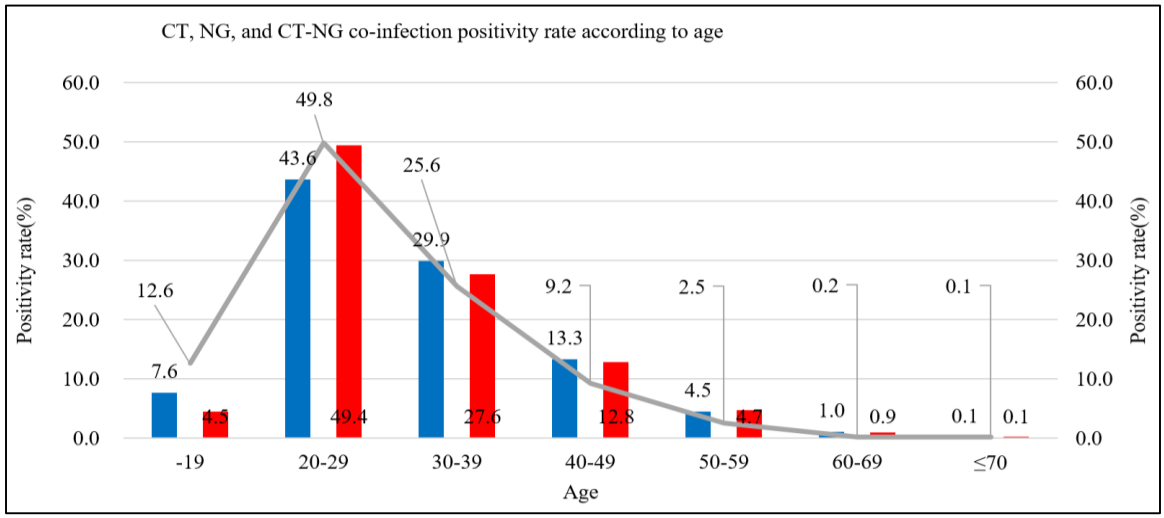

Fig. 3: Positivity ratios for CT and NG infection and co-infection by age group (-19≤70 years) Blue bars represent *Neisseria gonorrhoeae* (NG) positivity rates and red bars represent *Chlamydia trachomatis* (CT) positivity rates. The line graph shows the rate of CT and NG co-infection. The left y-axis corresponds to the bar graph values, while the right y-axis corresponds to the line graph values. The x-axis represents the age groups

Discussion

We analyzed sex- and age-based statistics to conduct a comprehensive statistical analysis of STD co-infection rates and possible relationships between pathogens to enhance our understanding of health and hygiene through sex- and age-based statistics. The prevalence of STD-causing agents varies with age (Kim, 2013; Agwu, 2020; Lee *et al*., 2022); however, the prevalence of each pathogen does not uniformly change (Kim, 2013; Agwu, 2020). We found that the proportion of males co-infected with CT and NT increases with age, peaking in the 20-30 age group, and is strongly associated with CT infection (Seo *et al*., 2021). We observed higher positivity rates for both CT and NG in males than in females, with younger individuals showing a greater susceptibility to STDs than older individuals (Park *et al*. 2018), which is likely due to more frequent partner changes (Svigals *et al*., 2020; Sedeh *et al*., 2021). Additionally, the probability of reinfection after an initial STD was found to be higher than the likelihood of first-time infection (Upton *et al*., 2018). In terms of sex, the STD positivity rate was higher in males (Seo *et al*., 2021). These findings suggest that sex and frequent partner changes in younger age groups contribute to variations in STD positivity rates.

CT and NG are common pathogens transmitted via sexual contact (Hocking *et al*., 2013; Lanjouw *et al*., 2016). Their distribution patterns are influenced more by lifestyle factors than by education or economic background, aligning with the higher STD susceptibility observed in younger age groups. Previous studies (Kim, 2013; Park *et al*., 2018; Seo *et al*., 2021; Lee *et al*., 2022) have reported that the mean age of females testing positive for STDs is approximately 31.9 years, with higher positivity rates in younger groups (Park *et al*., 2018). Our study confirmed that younger age groups (excluding those under 19 years) had the highest STD positivity rates, particularly in the 20–29 age group. For NG infections, males exhibited less stable infection vulnerability compared with females. Literature shows inconsistent sex-based differences in STD positivity (Seo *et al*., 2021), but generally, males are more prone to bacterial infections and may experience differences in healthcare access and treatment adherence than females (Dias *et al*., 2022). Another study revealed that the risk of infection in females could increase if the infections are asymptomatic and remain untreated (Dubbink *et al*., 2018).

Our study corroborates that susceptibility to disease transmission varies by sex and that asymptomatic infections affect overall positivity rates.

The sensitivity of CT and NG diagnosis using vaginal swabs collected by both clinicians and patients was 95%, with no significant difference in the positivity rates between the two collectors. For CT, the positivity ratio match rate was >90%, whereas for NG, it was >88%. Our findings support the use of swab collection methods due to their higher sensitivity compared to urine collection (Sedeh *et al*., 2021). Furthermore, because co-infections are common in venereal diseases, tests that can detect multiple pathogens should be conducted (Lau and Ho, 2023). We used a molecular biological testing method to examine pathogen plurality, and the positivity rate was higher with the swab collection method than with the urine collection method, allowing us to observe sex-

related differences. Although patients often prefer a less invasive urine collection method, swab collection offers superior accuracy, as confirmed by other studies. For example, CT detection showed 93% sensitivity with cotton swabs and 78% with urine analysis, which further confirmed the differences in sensitivity between the cotton swab method and urine test (Yared *et al*., 2018). The higher positivity rates observed with swab samples, despite their lower collection ratios, validate the use of swabs for accurate STD testing.

Conclusion

This study provides valuable insights into CT and NG co-infections, and the results can be used to develop future prevention and management strategies for STDs. Through a retrospective analysis of STD positivity rates based on factors such as sample collection methods, sex, and age, we highlight the importance of accurate testing and targeted prevention measures. However, our analysis was limited by the variability in sample collection between males and females and the data available. To gain a more comprehensive understanding of pathogen interactions and enhance public health strategies, future research should investigate trends in co-infections and other STDs over time.

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Author's Contributions

Hyeok-Jin Kwon, Sun-Gyu Kim and Jae Kyung Kim: Made substantial contributions to the conception and design of the study, the analysis of the data, the preparation and critically review of manuscript, and the final approval of the submitted and revised manuscript versions.

Junmin Lee and Dongin Seok: Made substantial contributions to the conception and acquisition of the data, the preparation and critical review of manuscript, and the final approval of the submitted and revised manuscript versions.

Ethics

This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the Clinical Research Review Committee of Dankook University (Institutional Review Board DKU, Certificate No. DKU 2021-04-002).

Conflict of Interest

The authors declare that they have no conflict of interest.

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