INTRODUCTION

Sexually transmitted infections (STIs) are caused by pathogens commonly transmitted through sexual contact, particularly vaginal, anal, or oral sex.1,2 STIs continue to be a serious problem. The global incidence remains high, but most STIs are asymptomatic.3 It is estimated that more than 500 million people between the ages of 15 and 49 years have genital infections caused by the herpes simplex virus (HSV).3 Pathogens that cause STIs include bacteria, parasites, and viruses.4 Bacterial STIs include chlamydia, gonorrhea, and syphilis;
parasitic STIs include trichomoniases; and viral STIs include human immunodeficiency virus, HSV, and hepatitis B virus infection. They cause symptomatic or asymptomatic infections of genital organs, which may lead to infertility, pregnancy complications, cancer, and even death. If left untreated, STIs can have serious consequences, including neurological manifestations, infertility, mother-to-child transmission, and birth defects.

Various methods are used to diagnose STIs, including culture or serological tests for each specific pathogen, but these methods are generally time-consuming and lack sensitivity for identifying STIs in asymptomatic patients. Considering the frequency of coinfection with STIs, the high number of asymptomatic cases, and the difficulties associated with culture methods, nucleic acid amplification testing is an appropriate method for diagnosing STIs. Multiplex polymerase chain reaction (mPCR) is a sensitive and rapid method for simultaneous detection of STIs caused by multiple pathogens in clinical laboratories and has recently attracted attention as a method for detecting sexually transmitted pathogens using molecular diagnostics.

A significant proportion of patients with STIs are coinfected with multiple pathogens. In this study, patients were tested for coinfections with 12 different sexually transmitted pathogens: Candida albicans, Chlamydia trachomatis, Gardnerella vaginalis, HSV1, HSV2, Mycoplasma genitalium, Mycoplasma hominis, Neisseria gonorrhoeae, Treponema pallidum, Trichomonas vaginalis, Ureaplasma parvum, and Ureaplasma urealyticum. A symbiotic relationship between T. vaginalis and M. hominis has been reported in a Chinese study. A novel Mycoplasma strain, Candidatus Mycoplasma girerdii, has been identified in vaginal secretions of women, and it has been shown that this strain may be associated with trichomoniases. In Madrid, Spain, T. vaginalis was shown to play a key role in the risk of acquiring infections with other genitourinary pathogens, such as N. gonorrhoeae and C. trachomatis. M. genitalium, which is considered an independent risk factor for cervicitis in women, was found only in C. trachomatis-positive samples. A study conducted in Croatia also showed a significant association between M. genitalium and C. trachomatis infections. M. genitalium and M. hominis infections have also been reported to be significantly associated.

The number of STIs continues to increase worldwide. Although there are multiple reports on STIs caused by multiple pathogens, there is little information on the frequency of STIs with multiple pathogens according to age. Therefore, this study aimed to investigate the trend of coinfection by age in patients in the Republic of Korea screened for STIs using mPCR from 2018 to 2020.

2 | MATERIALS AND METHODS

2.1 | Materials

From January 2018 to December 2020, 65,191 samples of swab, urine, and other types (catheter, pus, and tissue) from patients who were tested for STIs, excluding those aged 0 and over 100 years old, were obtained from U2Bio Co. Ltd. (Seoul, Republic of Korea) for STI screening.
The prevalence of coinfection differed according to the sexually transmitted pathogen type. Among them, *N. gonorrhoeae* and *C. trachomatis* showed a high rate of single infection but a low rate of coinfection, and *N. gonorrhoeae* showed the lowest rate of coinfection with two or more other sexually transmitted pathogens. Conversely, *M. hominis* showed a low rate of single infection and a high rate of coinfection. Among patients with *M. hominis* or *T. vaginalis* infections, the majority had coinfections with more than two types of pathogens (Figure 2).

4 | DISCUSSION

This study showed that the rate of coinfection with multiple pathogens differed according to the age group and that it was higher in younger individuals. A previous study from China reported a high prevalence of STIs in adults between the ages of 20 and 39 years. This is because young adults have a lower level of awareness of the risks associated with sexual activity and may engage in sexual activity with multiple sexual partners and unprotected sex. In addition, according to a study conducted in New Mexico, the USA, the

### TABLE 1 Number of specimens that tested positive for each type of sexually transmitted pathogen (*N* = 35,366)

| Pathogen               | Number of positive specimens |
|------------------------|------------------------------|
| *Candida albicans*     | 2068                         |
| *Chlamydia trachomatis*| 4674                         |
| *Gardnerella vaginalis*| 22,747                       |
| Herpes simplex virus 1 | 194                          |
| Herpes simplex virus 2 | 1358                         |
| *Mycoplasma genitalium*| 2118                         |
| *Mycoplasma hominis*   | 3527                         |
| *Neisseria gonorrhoeae*| 1638                         |
| *Treponema pallidum*   | 22                           |
| *Trichomonas vaginalis*| 182                          |
| *Ureaplasma parvum*    | 11,521                       |
| *Ureaplasma urealyticum*| 9330                       |

### TABLE 2 Rates of coinfection with each sexually transmitted pathogen

|          | NG   | CT   | UU   | MG   | MH   | TV   | GV   | Candida | UP   | TP   | HSV 1 | HSV 2 |
|----------|------|------|------|------|------|------|------|---------|------|------|-------|-------|
| Single   | 32.01| 32.15| 39.16| 33.32| 39.85| 45.55a| 40.54| 43.55   | 40.11| 30.29| 32.66 | 42.37 |
| 2 types  | 29.48| 29.64| 37.35| 31.20| 39.73| 46.53| 39.31| 39.14   | 39.61| 29.00| 32.92 | 38.57 |
| 3 types  | 29.33| 28.86| 37.14| 31.09| 38.75| 40.76| 37.63| 37.58   | 37.87| 35.00| 32.91 | 38.39 |
| 4 types  | 28.39| 28.76| 35.24| 29.23| 35.61| 40.30| 34.60| 33.93   | 35.04| 27.75| 26.38 | 36.95 |
| 5 types  | 25.63| 26.06| 31.30| 25.81| 30.91| 45.47| 30.51| 29.87   | 31.41| 24.50| 36.57 |
| 6 types  | 23.50| 24.50| 25.97| 26.82| 24.51| 25.80| 25.81| 25.32   | 25.88| N/D  | 28.00 | 30.53 |
| 7 types  | N/D  | 23.00| 23.00| 22.00| 23.00| N/D  | 23.00| 23.50   | 23.00| N/D  | 23.00 | 23.00 |
| 8 types  | N/D  | N/D  | N/D  | N/D  | N/D  | N/D  | N/D  | N/D     | N/D  | N/D  | N/D   | N/D   |
| 9 types  | 19   | 19   | 19   | N/D  | 19   | 19   | N/D  | 19      | N/D  | 19   | 19    | N/D   |

Abbreviations: Candida, *Candida albicans*; CT, *Chlamydia trachomatis*; GV, *Gardnerella vaginalis*; HSV1, Herpes simplex virus 1; HSV2, Herpes simplex virus 2; MG, *Mycoplasma genitalium*; MH, *Mycoplasma hominis*; N/D, Not Detected; NG, *Neisseria gonorrhoeae*; TP, *Treponema pallidum*; TV, *Trichomonas vaginalis*; UP, *Ureaplasma parvum*; UU, *Ureaplasma urealyticum*.

*Highest percentage.*
highest rate of coinfection with *M. genitalium*, *C. trachomatis*, and *T. vaginalis* occurred in women aged 20–29 years and decreased with increasing age.13 In this study, the rate of coinfections differed according to sex. In males, the rate of coinfection was the highest in the 30- and 39-year age group, but in females, the age trend was less marked. According to a study on women of childbearing age conducted in South Africa, coinfections (*T. vaginalis* and *C. trachomatis*, or *T. vaginalis* and *N. gonorrhoeae*) were mainly observed in women under the age of 30 years.14 Moreover, according to another study conducted in South Africa, the prevalence of coinfection was 56.2% among women with bacterial vaginosis, and 53.4% among women with nonulcerative STIs, with an average age of 26 years.15 This study showed that the rate of coinfection varied according to the pathogen type. Patients with *N. gonorrhoeae* and *C. trachomatis* infection had a low rate of coinfection, whereas those infected with *M. hominis* and *T. vaginalis* had a high rate of coinfection with other sexually transmitted pathogens. A study conducted in an STI clinic in Birmingham, Alabama, USA, found that coinfection with *M. genitalium* in women with *C. trachomatis* was uncommon, and that it was present in only 7.3% of the coinfection patients.16 A study of pregnant women who visited a hospital in Ghana showed that *Candida* (53%) coinfection was common in women with *T. vaginalis* infection.17 In addition, in another study from Iran in which coinfection with sexually transmitted pathogens was confirmed using mPCR, 10/300 patients (3.3%) tested had coinfections confirmed, including 2 cases of *C. trachomatis*/*N. gonorrhoeae*, 3 cases of *C. trachomatis*/*T. vaginalis*, and 5 cases of *N. gonorrhoeae*/*T. vaginalis* coinfections.7 According to a study conducted in Beijing, China, among the patients with coinfections, 60.6% of men and 71.4% of women were coinfected with *U. urealyticum* and *C. trachomatis*.2 This study has several limitations. First, it is not possible to determine the characteristics of the sexual partner (same-sex or opposite-sex, occupation, or education level). Second, as this was a retrospective study that used laboratory records, we did not have data on the clinical characteristics of the patients. In this study, data on coinfection with STIs were collected and analyzed by age and bacterial species. These results could help public health managers recognize and prevent STIs in various age groups. Therefore, the study results can be used for educational purposes and to develop public health policies related to STIs by recognizing the differences in the STI profile according to age group.

**FUNDING INFORMATION**
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

**CONFLICT OF INTEREST**
The authors declare that there is no conflict of interest.

**DATA AVAILABILITY STATEMENT**
The datasets used or analyzed during the current study are available from the corresponding author upon reasonable request.

**ORCID**
Jae-Sik Jeon (https://orcid.org/0000-0001-8981-5705)
Jae Kyung Kim (https://orcid.org/0000-0002-1534-563X)

**REFERENCES**
1. US Centers for Disease Control and Prevention. Sexually Transmitted Infections Treatment Guidelines. 2021. [https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf](https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf). Accessed 28 May 2022.
2. Liang Y, Zhai H, Li Z, et al. Prevalence of *Ureaplasma urealyticum*, *chlamydia trachomatis*, *Neisseria gonorrhoeae* and herpes simplex virus in Beijing, China. *Epidemiol Infect.* 2021;147:E59.
3. World Health Organization. Sexually transmitted infections (STIs). 2021. [https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis)](https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis)). Accessed 28 May 2022.
4. Barrientos-Durán A, de Salazar A, Alvarez-Estévez M, Fuentes-López A, Espadafor B, Garcia F. Detection of sexually transmitted disease-causing pathogens from direct clinical specimens with the multiplex PCR-based STD direct flow Chip kit. *Eur J Clin Microbiol Infect Dis.* 2020;39:235-241.
5. Britto AMA, Policarpo C, Pezzuto P, et al. Detection of sexually transmitted infections at a Brazilian gynecology center: high prevalence of co-infections. *J Bras Patol Med Lab*. 2018;54:393-400.

6. World Health Organization. Four curable sexually transmitted infections still affect millions worldwide. 2019. https://www.who.int/news/item/05-06-2019-four-curable-sexually-transmitted-infections-still-affect-millions-worldwide. Accessed 28 May 2022.

7. Nateghi Rostami M, Hossein Rashidi B, Nazari R, Aghsaghloo F, Habibi A. A multiplex assay of *trichomonas vaginalis, chlamydia trachomatis* and *Neisseria gonorrhoeae* infections in genital specimens. *J Infect Dev Ctries*. 2017;11:833-839.

8. Chung HS, Lee M. Comparative evaluation of multiplex real-time PCR assays for six pathogens of sexually transmitted infections. *Ann Clin Microb*. 2017;20:1-6.

9. Xu S, Wang Z, Zhou H, Fu Y, Feng M, Cheng X. High co-infection rate of *trichomonas vaginalis* and *Candidatus mycoplasma Girerdii* in Gansu Province, China. *Healthcare (Basel)*. 2021;9:706.

10. Bolumburu C, Zamora V, Muñoz-Algarra M, Portero-Azorín F, Escario JA, Ibáñez-Escribano A. Trichomoniasis in a tertiary hospital of Madrid, Spain (2013–2017): prevalence and pregnancy rate, coinfections, metronidazole resistance, and endosymbiosis. *Parasitol Res*. 2020;119:1915-1923.

11. Ljubin-Sternak S, Mestrovic T, Kolaric B, Jarza-Davila N, Marijan T, Vranesh J. Assessing the need for routine screening for *mycoplasma genitalium* in the low-risk female population: a prevalence and co-infection study on women from Croatia. *Int J Prev Med*. 2017;8:51.

12. Visalli G, Cosenza B, Mazzù F, et al. Knowledge of sexually transmitted infections and risky behaviours: a survey among high school and university students. *J Prev Med Hyg*. 2019;60:E84-E92.

13. Hammer A, Gravitt PE, Adcock R, et al. Burden of *mycoplasma genitalium* and bacterial coinfections in a population-based sample in New Mexico. *Sex Transm Dis*. 2021;48:e186-e189.

14. Sethowa JS. *Trichomonas Vaginalis* and *Bacterial Co-Infections Identified in Reproductive Age Women*. Master’s Thesis. University of Pretoria; 2017.

15. Gumede L, Kufa-Chakezha T, Maseko V, et al. Predictors of sexually transmitted co-infections in women presenting with bacterial vaginosis to primary healthcare facilities in South Africa. *Sex Transm Infect*. 2017;93:A143.

16. Harrison SA, Olson KM, Ratliff AE, et al. *Mycoplasma genitalium* coinfection in women with *chlamydia trachomatis* infection. *Sex Transm Dis*. 2019;46:e101-e104.

17. Asmah RH, Blankson HNA, Seanefu KA, et al. Trichomoniasis and associated co-infections of the genital tract among pregnant women presenting at two hospitals in Ghana. *BMC Womens Health*. 2017;17:130.

How to cite this article: Lee SJ, Jang TS, Jeon J-S, Kim JK. Coinfections with multiple sexually transmitted pathogens in Republic of Korea, 2018–2020. *J Clin Lab Anal*. 2022;36:e24682. doi: [10.1002/jcla.24682](https://doi.org/10.1002/jcla.24682)