Original Research Article

Trend Analysis of the Profiles of 12 Sexually Transmitted Disease Pathogens in the Republic of Korea in 2019

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Abstract

Background: Sexually transmitted diseases (STDs) are common infectious diseases in humans transmitted through unprotected sexual activities. In South Korea, despite the high annual incidence of STDs, detailed examinations of pathogen-specific factors and causes for delays in diagnosis and treatment are still lacking. Furthermore, STD prevalence patterns and important pathogen-specific factors remain unclear. Herein, we retrospectively analyzed the epidemiology of STDs in South Korea in 2019 by analyzing the association of pathogen-specific infection patterns with factors such as sex, age, region, and month. Methods: We obtained the STD test results of 172,973 individuals from the Seoul Clinic Laboratory in 2019, most of whom had multiple infections; hence, 275,296 STD-positive cases were included in this analysis. Through deoxyribonucleic acid (DNA) amplification, they were categorized by pathogen type. Subsequently, they were further classified by month, region, and age while concurrently being stratified according to sex. Results: Among the 12 pathogens detected in this study, *Gardnerella vaginalis* had the highest prevalence, with 92,490 cases in both sex groups; moreover, many of them were concurrently infected by two or more pathogens. The prevalence of STDs did not differ according to month or region. Conversely, the pathogen-specific prevalence rates significantly differed according to age. Older adults had higher prevalence rates of *Chlamydia trachomatis*, *Trichomonas vaginalis*, *Candida albicans*, and herpes simplex virus type 1 infections than younger adults. Conclusion: These pathogen-specific prevalence patterns provide information that helps to understand population vulnerability according to region and age and helps develop STD prevention and treatment strategies in South Korea.

Keywords

age, region, sex, South Korea, STD

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What do we already know about this topic?
In South Korea, the Korea Centers for Disease Control and Prevention released data showing that the number of individuals with sexually transmitted diseases (STDs) is increasing every year, predicting a scenario that may lead to severe issues, considering the high infectivity rates of these diseases.

How does your research contribute to the field?
Our study elucidates the prevalence of STDs according to the time of the year, region, sex, and age, providing data that helps understand the epidemiology of STDs in South Korea.

What are your research's implications toward theory, practice, or policy?
The information regarding main pathogens of interest according to different factors is useful for the development of strategies to manage and control STDs.

Introduction

Sexually transmitted diseases (STDs), also known as sexually transmitted infections, spread from person to person through unprotected sexual activities. They represent the most common infectious diseases in the United States, with 20 million new cases estimated yearly.[1] Many studies have indicated that the number of patients with STDs has increased yearly, thus increasing public health concerns associated with these diseases.[2] In South Korea, the Korea Centers for Disease Control and Prevention released data showing that the incidence is increasing every year, predicting a scenario that may lead to severe issues considering the high infectivity rates of these diseases.[3]

STDs are caused by over 20 microorganisms comprising bacteria, viruses, and parasites.[4] Among the microorganisms, 12 pathogens—*Candida albicans*, *Chlamydia trachomatis*, *Gardnerella vaginalis*, *Mycoplasma genitalium*, *Mycoplasma hominis*, *Neisseria gonorrhoeae*, *Ureaplasma parvum*, *Ureaplasma urealyticum*, *Treponema pallidum*, *Trichomonas vaginalis*, herpes simplex virus type 1, and herpes simplex virus type 2—are recognized as the main causative pathogens or harbingers of STDs in South Korea, with some causing severe infections. Although previous studies have provided valuable information, they included limited subject population or risk factors. Moreover, no studies have investigated the relative frequency of the 12 main pathogens and examined their prevalence according to factors, such as time of year, region, or age.

In this study, we investigated the epidemiology of STDs in South Korea to understand pathogen-specific factors that may aid efforts to prevent these diseases. Subsequently, we studied the prevalence of STDs according to the time of year, region, sex, and age to provide data to assist in timely disease treatment and control measures.

Materials and Methods

Study Design

We obtained STD test results from the Seoul Clinic Laboratory (SCL) and classified them according to pathogen type, sex, time of year, region, and age. Patients using the SCL provided written informed consent for the use of their test results and information prior to their enrollment in this study. They were mostly outpatients who visited the health examination center for diagnosis or a routine health check. We confirmed STD test results through DNA amplification from various samples, including urine, cervical swab, semen, prostate, urethra, or cervix cells, using multiplex RT-polymerase chain reaction (PCR). We designed a classification for STD test results based on several factors. First, they were categorized according to pathogen type and sex. Subsequently, they were further classified by month, region, and age while concurrently being stratified according to sex.

DNA Extraction and Multiplex Real-Time Polymerase Chain Reaction

We acquired samples collected in 2019 from the SCL for this analysis and 172,973 individuals had 12 STD pathogens test at a time. We referred each one was as case. Approximately 2 million cases were classified according to pathogen type, sex, month, region, and age. Each collected sample had its DNA status tested using multiplex real-time PCR to detect STD-related pathogens. Epidemiological data were obtained by a retrospective clinical analysis. We included 275,296 STD-positive cases in this analysis from the 172,973 individuals, most of whom had multiple cases of STDs.

DNA samples from urine, cervical swabs, semen, prostate, urethra, or cervix cells were extracted using the MagNA Pure 96 DNA and Viral NA Large Volume Kit (Roche, Basel, Switzerland) according to the manufacturer's instructions. Subsequently, the extracted DNA samples underwent analysis for STD-related pathogen detection with the careGENE^{TM} STD-12 detection kit (WELLS BIO, Seoul, South Korea) using a CFX96 Real-Time PCR Detection System (Bio-Rad, Hercules, CA, US). Briefly, we prepared 15 µl of the master mix by mixing 10 µl of 2X reaction mixture and 5 µl of the set primer/probe mix. Each set primer/probe mix detected four types of STD-related pathogens and provided an internal control. Subsequently, 5 µl of the extracted DNA sample was analyzed using PCR. First, the predenaturation step was executed at 96°C for 15 min; then, 40 cycles of amplification were repeated at 94°C for 30 s and at 60°C for 1 min. We considered cycle threshold

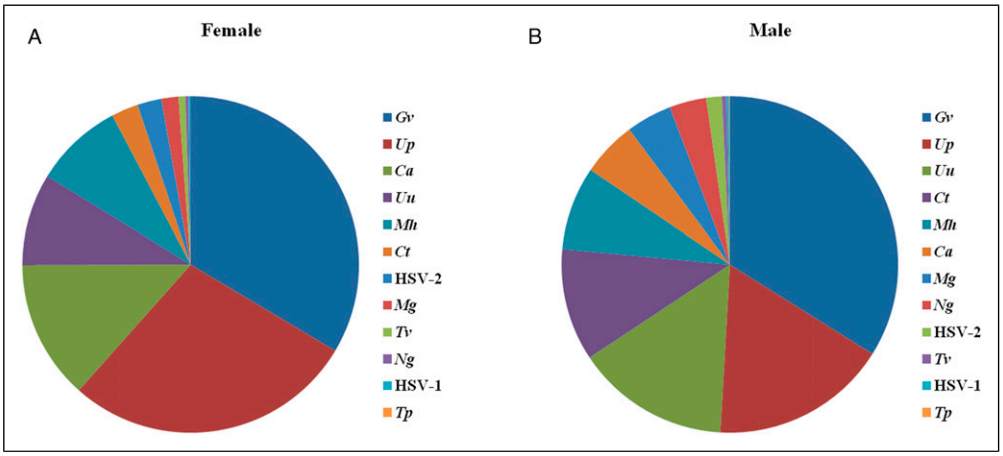

Figure 1. Infection distribution of each pathogen in South Korea in 2019. Among 275,296 STD cases, 243,834 were detected in female patients (A) and 31,462 were detected in male patients (B). The 12 pathogens are as follows: *Candida albicans* (*Ca*), *Chlamydia trachomatis* (*Ct*), *Gardnerella vaginalis* (*Gv*), *Mycoplasma genitalium* (*Mg*), *Mycoplasma hominis* (*Mh*), *Neisseria gonorrhoeae* (*Ng*), *Ureaplasma parvum* (*Up*), *Ureaplasma urealyticum* (*Uu*), *Treponema pallidum* (*Tp*), *Trichomonas vaginalis* (*Tv*), herpes simplex virus type 1 (HSV-1), and herpes simplex virus type 2 (HSV-2).

values <39 as positive results and those ≥39 or not available as negative results.

Ethical Considerations

This study was approved by the Institutional Review Board of the Seoul Clinic Laboratory, Republic of Korea (IRB-21-007-01). All participants provided written informed consent.

Results

Analysis of Sexually Transmitted Diseases-Related Pathogen Infection Pattern According to Sex

To understand the infection pattern of STDs, we examined data of 172,973 patients using multiplex real-time PCR to detect 12 pathogens and obtained approximately 2 million results. Among all the cases, 275,296 positive cases were included in our analysis. PCR was used to simultaneously detect the 12 pathogens—*Candida albicans*, *Chlamydia trachomatis*, *Gardnerella vaginalis*, *Mycoplasma genitalium*, *Mycoplasma hominis*, *Neisseria gonorrhoeae*, *Treponema pallidum*, *Trichomonas vaginalis*, *Ureaplasma parvum*, *Ureaplasma urealyticum*, herpes simplex virus type 1, and herpes simplex virus type 2 (Supplementary Figure 1). Figure 1 shows the incidence of STD pathogens according to sex in 2019. The graph showed a high prevalence of positive cases. Among the pathogens, *Gardnerella vaginalis* was the most prevalent among female and male patients, with 81,820 and 10,670 positive cases, respectively, followed by *Ureaplasma parvum* (women: 68,312 cases; men: 5,347 cases) (Figure 1, Supplementary Table 1). Among female patients, *Candida albicans*, the pathogen causing candidiasis on the skin or mucous membranes of the body, and *Ureaplasma urealyticum*, the pathogen associated with urogenital infections that may lead to infertility, had the third and fourth highest prevalence rates, respectively, (Figure 1).[5] Among male patients, *Ureaplasma urealyticum* and *Chlamydia trachomatis*—a pathogen associated with trachoma, oculo-genital, and neonatal infections—had the third and fourth higher prevalence rates, respectively.[6]

Furthermore, the number of pathogen-positive cases exceeded the number of patients due to recurrence of STDs (Supplementary Table 1). Therefore, we investigated the rate of multiple STDs according to sex and found that 67.59% and 46.93% of female and male patients, respectively, were concurrently infected by two or more pathogens (Table 1). Additionally, a small proportion (0.01%) of female patients were concurrently infected by eight pathogens.

Analysis of Sexually Transmitted Diseases-Related Pathogen Infection Pattern According to Other Factors

To examine STD characteristics, we analyzed the results according to the time of year (month), region, and age. Regarding the time of year, the infection rates with respect to the months appeared similar between female and male patients (Supplementary Figure 2). Like in the analysis stratified by sex, *Gardnerella vaginalis* and *Ureaplasma parvum* displayed high infection rates throughout the months for both sex groups. Among the female patients, *Ureaplasma urealyticum* and *Mycoplasma hominis* infections slightly declined from June to December; conversely, *Candida albicans* infection increased in the same period (Supplementary Figure 2(a)). Similarly, among the male patients, *Mycoplasma hominis* and *Mycoplasma genitalium* infections slightly declined from June to December, with an increase in *Candida albicans* infection in the same period (Supplementary Figure 2(b)).

We included 42 cities in South Korea, which were categorized into nine groups to designate the provinces of Seoul, Gyeonggi-do, Gangwon-do, Chungcheong-do, Gyeongsangbuk-do, Gyeongsangnam-do, Jeollabuk-do, Jeollanam-do, and Jeju

Table 1. Patients with Multiple STDs According to the Concurrent Number of Detected Pathogens and Sex.

Number of Identified Pathogens	Female Patients	Male Patients	Multiple Infection Percentage (%)	
			Female Patients	Male Patients
1	36,922	10,082	32.41	53.07
2	39,858	6,069	34.98	31.95
3	25,091	2,248	22.02	11.83
4	9,079	503	7.97	2.65
5	2,385	85	2.09	0.45
6	492	9	0.43	0.05
7	94	1	0.08	0.01
8	9	—	0.01	—

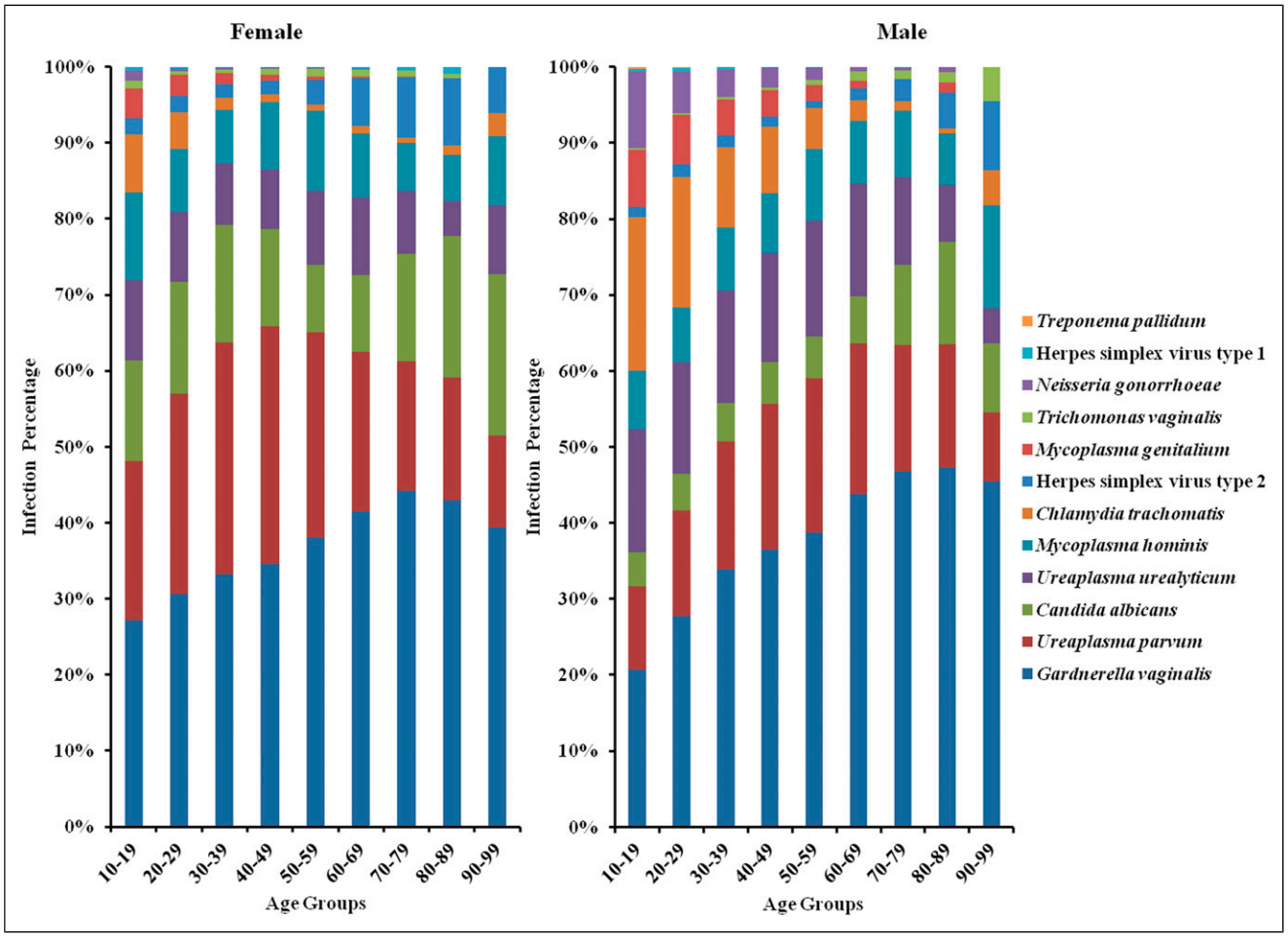

Figure 2. Infection percentages of each pathogen according to age groups. The *X*-axis represents age groups (years), and the *Y*-axis represents the infection percentage of total STD-positive cases.

Island (Supplementary Figure 3(a)). We found no considerable difference in infection across the provinces (Supplementary Figures 3(b) and (c)).

Finally, regarding age, we first excluded individuals younger than 10 years and those with missing age information; hence, 250,541 positive cases (91% of total cases) were included in this study. Figure 2 illustrates how the rates of pathogen infections differed according to age groups. The infection patterns in male and female patients were similar. Specifically, the *Chlamydia trachomatis* infection

rate decreased in the 10–19-year age group and higher but increased in the 80-year or older age group. *Neisseria gonorrhoeae* and *Mycoplasma hominis* infection rates declined as age increased and these pathogens rarely infected older adults (≥70 years). In contrast, *Candida albicans* and herpes simplex virus type 1 infections increased with age.

Discussion

STDs are serious infections that cause diverse illnesses with varied symptoms in humans worldwide. The incidence of STDs increases each year, highlighting the need for studies to develop efficient prevention and treatment strategies. Few studies on STDs have originated from South Korea, and these studies included limited population groups, pathogens, or regions. Therefore, it is important to investigate the actual prevalence of STDs in Korea. This is the first study to include individual infection percentages of 12 main STD-related pathogens and explore differences in region, time of year, age, and sex.

Our results showed that the number of infected female patients was higher than that of infected male patients, indicating that women were more vulnerable to STDs than men. Similarly, previous studies reported that STDs impact both sexes differently and pose a greater threat to women's health because of the structural differences in genital organs.[7] In the US, the Centers for Disease Control and Prevention reported that women are at a greater risk because infections occurring in the vagina may not be readily visible, and some STD-related pathogens may be transmitted vertically (from mother to child). Thus, regular health check-ups, regardless of the presence of symptoms or signs of disease, are very important to prevent and identify STDs early.

Our study also evaluated the occurrence of multiple STDs. The co-occurrence of two or more pathogens was detected in 132,927 patients, indicating a considerably high percentage of multiple STDs in this population (Table 1). In South Korea, the number of pathogens included in tests for STDs is relatively higher, and check-ups are performed more often than in other countries. These factors may contribute to the high percentage of multiple STDs observed in this study, including instances of eight concurrent pathogen infections. Most patients with multiple infections were reported to have *Gardnerella vaginalis* and *Ureaplasma parvum* among the detected pathogens (data not shown). Nonetheless, multiple STDs are more challenging to treat than singular infections, and they indicate an increased risk for HIV transmission.[8] Thus, effective and timely treatment of multiple STDs requires accurate diagnosis to confirm the multiple infection status.

We analyzed infection percentages according to age, time of year, and region to account for different environmental and lifestyle factors. We observed that the infection rates of pathogens were similar across different climate conditions (e.g., high temperatures and humidity of summer or cold wave of winter) and regions (i.e., provinces) (Supplementary Figures 2 and 3, and Supplementary Tables 2 and 3). We hypothesized that this similarity was because of the relatively stable controlled climatic conditions in interior environments, which reduces the impact of seasonality on the body, such as alterations in temperature or pH.[9] Moreover, South Korea is relatively small, and the transit system is sufficiently developed to travel across the country in one day, narrowing the gap between regions. Particularly, in Gyeongsangnam-do, the number of positive cases seems higher than those in other regions (Supplementary Table 3), while the infection rate was similar to those in other regions. Additionally, the number of negative cases was high in this region (data not shown).

We observed notable characteristics in the age group analysis (Figure 4 and Supplementary Table 4). According previous study, *Chlamydia trachomatis* had a high re-infectivity rate, and 50% and 80% of infected women and men, respectively, were asymptomatic.[10] Thus, a high percentage of asymptomatic *Chlamydia trachomatis* infections often remain untreated, leading to constant re-infection.[11] Based on these study findings, we hypothesized that *Chlamydia trachomatis* infections remain untreated and colonize gradually over time, reaching higher infection rates in older adults. The same hypothesis applies to the *Trichomonas vaginalis*-age group infection pattern.[12] In addition, some studies reported that *Trichomonas vaginalis* and *Mycoplasma hominis* infections are closely associated.[13] Accordingly, our results showed that *Mycoplasma hominis* infection rates increased in older adults following an increase in *Trichomonas vaginalis* infection rates (Figure 2). Other bacterial interactions remain unknown and may pose additional threats to human health.

Among the 12 pathogens, *Neisseria gonorrhoeae* and *Mycoplasma hominis* have been extensively studied, leading to a relatively high cure achievement owing to developed treatment methods. However, microbes evolve constantly, causing antibiotic treatment failures.[14] Moreover, concurrent *Neisseria gonorrhoeae* and *Mycoplasma genitalium*, and *Candida albicans* and herpes simplex virus type 1 exhibit resistance to drug treatments.[15] This acquired resistance to antibiotics allows pathogens to survive and continuously cause diseases. Therefore, it is important to elucidate pathogens' characteristics to diagnose and treat these infections accurately.

This study is an original survey on STD pathogens in the Republic of Korea. We highlighted the importance of a nationwide study with 12 common pathogens. The knowledge of the distribution of these common pathogens has a substantial public health implication for their prevention, identification, and treatment. For example, a recent study reported that *Chlamydia trachomatis* infection decreased during the COVID-19 pandemic[16]; the same findings were observed when compared with SCL's 2020 chlamydia-positive results. The number of chlamydia-positive cases in 2019 was 9,713, which decreased by approximately 17% (8,088) in 2020. The

reason is because the frequency of contact between people decreased due to the quarantine measures. In addition, infection due to not only *Chlamydia trachomatis* but also other pathogens is expected to decrease in 2020. This way, data gathered over several years will be utilizable in identifying the incidence patterns.

However, the study had some limitations. First, the correlation with prevalence and behaviors could not be identified because detailed information on a lifestyle or sex life of individual was lacking. Second, the information regarding the prevalence in many regions remains unclear and, as there were only results from 2019, the pattern of infectious bacteria could not be expected. Therefore, further research is required to investigate re-infection and to determine trends. We will continue to accumulate test results including those on re-infection for public health, and to establish a way to prevent STDs by identifying outbreak patterns.

In conclusion, our results indicated that seasonality and region did not affect pathogen infection patterns when stratified by sex; infection patterns varied according to age. These results, especially the information regarding main pathogens of interest according to different factors, are useful for the development of strategies to manage and control STDs. Moreover, to the best of our knowledge, this was the first study to include 12 pathogens using a nationally representative data in South Korea, thus providing a foundation to develop better strategies and new insights for managing and treating STDs.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval

The study was approved by the Institutional Review Board of the Seoul Clinic Laboratory, Republic of Korea (IRB-21-007-01). All participants provided written informed consent.

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Supplemental Material

Supplemental material for this article is available online.

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