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Spatiotemporal Clusters and Trend of *Trichomonas vaginalis* Infection in Korea

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Abstract: This study was done to provide an overview of the latest trichomoniasis status in Korea by finding disease clusters and analyzing temporal trends during 2012-2020. Data were obtained from the Health Insurance Review & Assessment Service (HIRA) of Korea. SaTScan and Joinpoint programs were used for statistical analyses. Gyeonggi-do had the highest average population and highest number of cases. The high incidence of *T. vaginalis* infections were observed among women aged 40-49 and 30-39 years (33,830/year and 33,179/year, respectively). Similarly, the 40-49 and 30-39 age group in men showed the highest average cases (1,319/year and 1,282/year, respectively). Jeollabuk-do was the most likely cluster, followed by Busan/Gyeongsangnam-do/Ulsan/Daegu and Jeju-do and Gwangju. Urban and rural differences were prominent. Trichomoniasis has decreased significantly in most clusters, except for Incheon. Trichomoniasis was decreasing in women recently after peaking around 2014. Men showed different trends according to age. Trichomoniasis was increasing in the 10-39 age groups, but decreasing in the 40-59 age groups. This study might provide an analytic basis for future health measures, policy-makers, and health authorities in developing effective system for prevention of trichomoniasis.

Key words: Trichomonas, HIRA, cluster, trend, spatial analysis, temporal analysis, SaTScan, Joinpoint

INTRODUCTION

Trichomoniasis is one of the most common sexually transmitted infection (STI) globally. The responsible pathogen, *Trichomonas vaginalis*, is a flagellate protozoan that infects the human vagina, prostate gland, and urethra [1]. The majority of women and men with trichomoniasis are asymptomatic [2,3], but it may cause vaginitis and cervicitis in women, and serious complications including infertility, preterm birth, and pelvic inflammatory disease [4,5]. Although the incidence is lower in men, it may cause nongonococcal urethritis, prostatitis, epididymitis, and infertility [6,7]. Cervical neoplasia [8] and prostate cancer are known to be associated with trichomoniasis [9]. It is also a high-risk factor for HIV and other STIs, and thus may pose a significant public health problem [10]. According to the WHO, 170 million people are believed to be

© 2022, Korean Society for Parasitology and Tropical Medicine This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited. infected annually, and it is more prevalent than *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and syphilis combined. Domestically, 10.4% of women complaining of vaginal symptoms and signs have been reported to be infected in Korea [11].

Korea has a complete full health-coverage of its population, and the clinical data from the Healthcare Bigdata Hub provided by the Health Insurance Review & Assessment Service (HIRA) of Korea has been used in this study, thereby representing the whole Korean population. Our study shows the results of a 9 year-survey.

We discuss the spatial infection clusters and infection trend present during this temporal window. SaTScan and Joinpoint programs were used to locate and statistically test these clusters and determine the most recent trend of trichomoniasis in Korea.

MATERIALS AND METHODS

Ethics statement

This study was performed under the regulation of the IRB Committee of The Catholic University of Korea (MIRB-2020 1127-002). This research adhered to the tenets of the Declara-

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tion of Helsinki.

Data Source and Definition

The nationwide trichomoniasis cases for 9 years (2012-2020) from the 17 administrative districts in Korea and ageperiod cohorts (5-year interval) according to sex were obtained from the HIRA of Korea. (https://opendata.hira.or.kr/home. do. [cited 2020 October]) The HIRA collects all relevant information from the records of all the patients at almost all hospitals and clinics in Korea, and the accuracy and reliability of its data have been systemically validated [12].

The population data of 17 administrative divisions 2012-2020 were obtained from the Korean Statistical Information Service (https://kosis.kr/index/index.do [cited 2021 October]). The geographical locations of the cases were set to the latitude and longitude of administrative center as the search point since the case data were compiled by administrative district unit. The population and number of cases were summed up as accumulated counts and numbers for the full period to evaluate overall trichomoniasis. Case numbers were adjusted for the particular district's population (cases/1,000,000) to facilitate comparison between the different districts (Table 1).

The cases were stratified into age groups, under 0-9, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, and 80 years and over, according to sex (Table 2). The total study period was evaluated initially, and it was further divided into tertiles (2012-2014, 2015-2017, 2018-2020) to evaluate the trend more specifically.

Spatiotemporal analyses of clusters and trend

SaTScan (v10.0) [13] was used to detect clusters and evaluate their significance through simulation. The discrete Poisson model was used since the case data were linked to their background population at risk. Spatial scan analysis detects clusters with maximum likelihood ratio by creating a circular window on a map and scanning the study area by varying the window size.

The window size determines a percentage of the population at risk within its boundaries [14]. Spatial scan statistic works best for detecting spatial clusters, and may be effective in the study of small numbered cases, such as novel or infrequent outbreaks [15,16]. It is important to find an appropriate set value of cluster size because a large value could hide the effect of small core clusters, while a small value could overlook the regional pattern of clusters [17]. Various studies have been performed to address this issue, and SaTScan has been progressively updated to address these results and implemented them on the new versions [18,19]. Therefore, we selected 50% window size for statistical analyses as per the users' guide in the present study.

General trend of the disease according to administrative districts was determined through spatial variation in temporal trend analysis, by scanning for clusters with either increasing or decreasing rates.

Statistical significance of the clusters was calculated using the Monte Carlo simulations with an inference of 9,999 [20] and expressed as *P*-value. A significance level of alpha < 0.05was used as a standard. QGIS software (v3.16) was used to visualize cluster patterns on a map. The clusters and trends are shown in order of log likelihood ratio. The study analyzed data from 2012 to 2020.

Trend analysis

Disease trend according to sex and age was determined using Joinpoint Regression Program (v4.9.0.0)(https://surveillance.cancer.gov/joinpoint/) [21,22], The present study used crude rates computed by the Joinpoint software, whereby the number of new cases occurring in a specified population per year is expressed as the number of cases per 100,000 population at risk.

A maximum number of 1 joinpoint was used, making it possible to see whether the incidence is better explained by a single trend or by the existence of multiple trend segments during the study period. Briefly, joinpoint regression identifies best-fitting break-points (years) in which there was a significant change in the incidence rate (crude rates) [23]. The results were summarized as annual percentage changes (APC) with the best model fit for each trend segment. Statistical significance was calculated with an inference of 9,999 and expressed as *P*-value. A significance level of alpha <0.05 was used as a standard.

The results were also output in graphs by the software, where crude rates and years are displayed. In some cases, the years are displayed twice, because the crude rates are calculated by midyear, and multiple trends reflect this aspect. The final selected models from statistically significant age groups according to sex were output into a single graph to view multiple models simultaneously.

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	Average						Cases					
	population	Total	2012	2013	2014	2015	2016	2017	2018	2019	2020	Average
Seoul (SE)	9,935,068	260,892	31,920	39,794	39,697	28,798	28,665	25,362	25,716	22,619	18,321	28,988
Busan (BU)	3,479,524	101,688	10,153	11,995	13,380	14,744	15,865	11,411	11,132	7,139	5,869	11,299
Incheon (IN)	2,922,033	60,760	5,638	6,364	6,246	6,963	7,170	7,928	7,933	8,145	4,373	6,751
Daegu (DG)	2,474,029	80,356	9,022	9,079	10,898	11,191	9,804	9,702	7,716	6,511	6,433	8,928
Gwangju (GW)	1,465,451	37,281	4,126	5,447	6,561	5,694	4,704	2,962	2,812	2,768	2,207	4,142
Daejeon (DJ)	1,505,918	22,801	2,047	3,172	3,444	3,295	3,703	2,783	2,016	1,591	750	2,533
Ulsan (UL)	1,157,860	31,765	3,209	2,946	3,341	4,070	4,707	3,791	3,464	3,549	2,688	3,529
Gyeonggi-do (GY)	12,726,986	270,493	24,131	33,382	35,730	35,062	32,439	32,086	29,050	26,477	22,136	30,055
Gangwon-do (GA)	1,544,798	18,998	2,461	2,553	2,494	2,022	2,234	2,001	2,287	1,868	1,078	2,111
Chungcheongbuk-do (CB)	1,587,489	30,868	3,809	3,966	4,149	4,143	4,874	3,212	2,528	2,440	1,747	3,430
Chungcheongnam-do (CN)	2,088,983	35,073	3,223	5,004	5,240	3,387	3,943	3,636	3,907	3,293	3,440	3,897
Jeollabuk-do (JB)	1,851,870	70,039	6,963	8,283	9,285	9,256	8,637	7,411	7,096	7,523	5,585	7,782
Jeollanam-do (JN)	1,892,796	19,681	2,764	2,695	2,316	1,761	2,634	2,198	1,828	1,999	1,486	2,187
Gyeongsangbuk-do (GB)	2,686,178	37,186	3,893	4,726	6,524	5,452	4,874	4,750	3,043	2,250	1,674	4,132
Gyeongsangnam-do (GN)	3,355,458	73,496	7,654	8,636	9,168	9,473	11,371	8,868	8,423	5,615	4,288	8,166
Jeju-do (JE)	635,639	26,737	2,948	3,466	3,262	2,998	2,921	2,736	2,916	2,881	2,609	2,971
Sejong (SJ)	237,329	391	14	25	13	18	69	42	69	63	78	43
Total	51,547,410	1,178,505	123,735	151,227	161,384	148,012	148,252	130,624	121,716	106,584	84,671	130,689
							Adjusted cases ⁶	t cases ^a				
			2012	2013	2014	2015	2016	2017	2018	2019	2020	Average
Seoul (SE)			3,131	3,923	3,929	2,873	2,887	2,573	2,633	2,325	1,895	2,908
Busan (BU)			2,869	3,400	3,802	4,196	4,535	3,288	3,235	2,091	1,730	3,238
Incheon (IN)			3,172	3,153	3,755	3,825	3,331	3,290	2,611	2,202	2,186	3,058
Daegu (DG)			2,250	2,544	2,505	2,799	2,886	3,203	3,222	3,341	1,808	2,729
Gwangju (GW)			2,808	3,698	4,445	3,868	3,202	2,024	1,927	1,900	1,522	2,822
Daejeon (DJ)			1,343	2,069	2,248	2,170	2,445	1,853	1,353	1,079	512	1,675
Ulsan (UL)			2,797	2,547	2,864	3,468	4,015	3,254	2,998	3,091	2,366	3,045
Gyeonggi-do (GY)			1,995	2,728	2,891	2,800	2,551	2,492	2,221	2,000	1,649	2,370
Gangwon-do (GA)			1,599	1,655	1,615	1,305	1,441	1,291	1,482	1,212	669	1,367
Chungcheongbuk-do (CB)			2,433	2,522	2,628	2,616	3,062	2,015	1,581	1,525	1,091	2,164
Chungcheongnam-do (CN)			1,589	2,444	2,541	1,630	1,881	1,718	1,837	1,551	1,622	1,868
Jeollabuk-do (JB)			3,717	4,422	4,961	4,950	4,632	3,996	3,863	4,136	3,096	4,197
Jeollanam-do (JN)			1,447	1,413	1,215	922	1,383	1,159	971	1,070	803	1,154
Gyeongsangbuk-do (GB)			1,443	1,751	2,416	2,017	1,805	1,765	1,137	844	634	1,535
Gyeongsangnam-do (GN)			2,306	2,590	2,737	2,815	3,370	2,623	2,496	1,670	1,284	2,432
Jeju-do (JE)			5,050	5,837	5,371	4,801	4,553	4,164	4,371	4,294	3,867	4,701
Sejong (SJ)			124	205	83	85	284	150	220	185	219	173
Total			2,429	2,957	3,144	2,872	2,868	2,523	2,349	2,056	1,634	2,537

^aAdjusted infection rate (cases/1,000,000).

RESULTS

General characteristics

A total of 1,178,505 trichomoniasis cases was reported, with an average of 130,689 cases/year during the study period of 2012 to 2020. Gyeonggi-do had the highest average population (12,726,986) and highest average number of cases (30,055). After adjusting for the population (cases/1,000,000), Busan had the highest average crude rate of 3,238. It also had the highest crude rate in 2016 at 4,535. Major cities tended to have a higher crude rate (Table 1).

The 40-49 and 30-39 age groups in women showed the highest average cases of trichomoniasis (33,830 and 33,179/year, respectively). Similarly, 40-49 and 30-39 age groups in men showed the highest average cases (1,319 and 1,282/year, respectively). After adjusting for the population (cases/1,000,000),

Table 2. Trichomoniasis and adjusted infection rate for 2012-2020 according to sex and age

	Age					Cases					– Average
	group	2012	2013	2014	2015	2016	2017	2018	2019	2020	- Average
emale	0-9	94	104	108	71	102	83	102	69	45	86
	10-19	2,923	3,407	3,611	3,063	3,135	2,900	2,722	2,250	1,806	2,869
	20-29	25,893	32,105	33,717	29,219	30,250	26,821	25,890	21,939	17,861	27,077
	30-39	32,159	39,862	43,634	39,300	38,680	32,364	29,251	24,647	18,712	33,179
	40-49	34,625	40,986	43,639	40,146	38,377	33,067	29,426	25,218	18,987	33,830
	50-59	18,847	24,284	25,761	24,898	24,551	22,390	21,341	19,282	15,550	21,878
	60-69	3,768	5,038	5,753	5,975	6,705	6,562	6,508	6,314	5,557	5,798
	70-79	1,000	1,480	1,744	1,762	1,845	1,702	1,737	1,649	1,485	1,600
	≥80	143	248	288	287	333	307	340	354	323	291
Nale	0-9	4	5	3	7	2	5	2	0	1	3
	10-19	40	29	33	52	58	47	42	46	64	46
	20-29	540	476	426	553	730	807	932	1,113	1,093	741
	30-39	1,159	1,106	1,081	1,052	1,472	1,448	1,371	1,527	1,325	1,282
	40-49	1,665	1,476	1,278	1,178	1,396	1,342	1,248	1,236	1,049	1,319
	50-59	1,258	1,182	982	932	1,033	1,006	990	1,049	815	1,027
	60-69	252	246	183	248	290	314	321	359	345	284
	70-79	51	46	34	55	58	69	62	64	65	56
	≥80	7	6	7	6	6	11	7	8	19	9
	Age				/	Adjusted cas	esa				
	group	2012	2013	2014	2015	2016	2017	2018	2019	2020	 Average
emale	0-9	42	46	48	32	46	38	49	34	23	40
Female						1 100		1 100			
	10-19	956	1,150	1,263	1,119	1,192	1,139	1,102	941	780	1,072
	10-19 20-29	956 8,175	1,150 10,233	1,263 10,699	1,119 9,214	1,192 9,458	1,139 8,322	8,010	941 6,798	780 5,525	1,072 8,493
								,			
	20-29	8,175	10,233	10,699	9,214	9,458	8,322	8,010	6,798	5,525	8,493
	20-29 30-39	8,175 8,029	10,233 10,157	10,699 11,404	9,214 10,476	9,458 10,505	8,322 9,001	8,010 8,248	6,798 7,165	5,525 5,617	8,493 8,956
	20-29 30-39 40-49	8,175 8,029 8,004	10,233 10,157 9,359	10,699 11,404 9,950	9,214 10,476 9,222	9,458 10,505 8,850	8,322 9,001 7,715	8,010 8,248 7,053	6,798 7,165 6,118	5,525 5,617 4,654	8,493 8,956 7,881
	20-29 30-39 40-49 50-59	8,175 8,029 8,004 4,862	10,233 10,157 9,359 6,095	10,699 11,404 9,950 6,317	9,214 10,476 9,222 6,031	9,458 10,505 8,850 5,895	8,322 9,001 7,715 5,320	8,010 8,248 7,053 4,990	6,798 7,165 6,118 4,483	5,525 5,617 4,654 3,631	8,493 8,956 7,881 5,292
	20-29 30-39 40-49 50-59 60-69	8,175 8,029 8,004 4,862 1,678	10,233 10,157 9,359 6,095 2,179	10,699 11,404 9,950 6,317 2,375	9,214 10,476 9,222 6,031 2,288	9,458 10,505 8,850 5,895 2,426	8,322 9,001 7,715 5,320 2,264	8,010 8,248 7,053 4,990 2,139	6,798 7,165 6,118 4,483 1,958	5,525 5,617 4,654 3,631 1,613	8,493 8,956 7,881 5,292 2,102
Лаle	20-29 30-39 40-49 50-59 60-69 70-79	8,175 8,029 8,004 4,862 1,678 580	10,233 10,157 9,359 6,095 2,179 835	10,699 11,404 9,950 6,317 2,375 966	9,214 10,476 9,222 6,031 2,288 973	9,458 10,505 8,850 5,895 2,426 1,007	8,322 9,001 7,715 5,320 2,264 897	8,010 8,248 7,053 4,990 2,139 892	6,798 7,165 6,118 4,483 1,958 829	5,525 5,617 4,654 3,631 1,613 730	8,493 8,956 7,881 5,292 2,102 857
Лаle	20-29 30-39 40-49 50-59 60-69 70-79 ≥80	8,175 8,029 8,004 4,862 1,678 580 182	10,233 10,157 9,359 6,095 2,179 835 296	10,699 11,404 9,950 6,317 2,375 966 319	9,214 10,476 9,222 6,031 2,288 973 295	9,458 10,505 8,850 5,895 2,426 1,007 320	8,322 9,001 7,715 5,320 2,264 897 277	8,010 8,248 7,053 4,990 2,139 892 288	6,798 7,165 6,118 4,483 1,958 829 280	5,525 5,617 4,654 3,631 1,613 730 242	8,493 8,956 7,881 5,292 2,102 857 278
Male	20-29 30-39 40-49 50-59 60-69 70-79 ≥80 0-9	8,175 8,029 8,004 4,862 1,678 580 182 2	10,233 10,157 9,359 6,095 2,179 835 296 2	10,699 11,404 9,950 6,317 2,375 966 319 1	9,214 10,476 9,222 6,031 2,288 973 295 3	9,458 10,505 8,850 5,895 2,426 1,007 320 1	8,322 9,001 7,715 5,320 2,264 897 277 2	8,010 8,248 7,053 4,990 2,139 892 288 1	6,798 7,165 6,118 4,483 1,958 829 280 0	5,525 5,617 4,654 3,631 1,613 730 242 0	8,493 8,956 7,881 5,292 2,102 857 278 1
Male	20-29 30-39 40-49 50-59 60-69 70-79 ≥80 0-9 10-19	8,175 8,029 8,004 4,862 1,678 580 182 2 12	10,233 10,157 9,359 6,095 2,179 835 296 2 2 9	10,699 11,404 9,950 6,317 2,375 966 319 1 1	9,214 10,476 9,222 6,031 2,288 973 295 3 17	9,458 10,505 8,850 5,895 2,426 1,007 320 1 20	8,322 9,001 7,715 5,320 2,264 897 277 2 2 17	8,010 8,248 7,053 4,990 2,139 892 288 1 1 16	6,798 7,165 6,118 4,483 1,958 829 280 0 18	5,525 5,617 4,654 3,631 1,613 730 242 0 26	8,493 8,956 7,881 5,292 2,102 857 278 1 1
Male	20-29 30-39 40-49 50-59 60-69 70-79 ≥80 0-9 10-19 20-29	8,175 8,029 8,004 4,862 1,678 580 182 2 12 12 156	10,233 10,157 9,359 6,095 2,179 835 296 2 9 138	10,699 11,404 9,950 6,317 2,375 966 319 1 11 122	9,214 10,476 9,222 6,031 2,288 973 295 3 17 157	9,458 10,505 8,850 5,895 2,426 1,007 320 1 200 205	8,322 9,001 7,715 5,320 2,264 897 277 2 77 2 17 225	8,010 8,248 7,053 4,990 2,139 892 288 1 16 259	6,798 7,165 6,118 4,483 1,958 829 280 0 18 311	5,525 5,617 4,654 3,631 1,613 730 242 0 26 306	8,493 8,956 7,881 5,292 2,102 857 278 1 16 209
Male	20-29 30-39 40-49 50-59 60-69 70-79 ≥80 0-9 10-19 20-29 30-39	8,175 8,029 8,004 4,862 1,678 580 182 2 182 2 12 156 278	10,233 10,157 9,359 6,095 2,179 835 296 2 9 138 270	10,699 11,404 9,950 6,317 2,375 966 319 1 11 122 271	9,214 10,476 9,222 6,031 2,288 973 295 3 17 157 268	9,458 10,505 8,850 5,895 2,426 1,007 320 1 200 205 382	8,322 9,001 7,715 5,320 2,264 897 277 2 277 2 277 225 384	8,010 8,248 7,053 4,990 2,139 892 288 1 1 6 259 368	6,798 7,165 6,118 4,483 1,958 829 280 0 18 311 421	5,525 5,617 4,654 3,631 1,613 730 242 0 242 0 26 306 374	8,493 8,956 7,881 5,292 2,102 857 278 1 16 209 335
Male	20-29 30-39 40-49 50-59 60-69 70-79 ≥80 0-9 10-19 20-29 30-39 40-49	8,175 8,029 8,004 4,862 1,678 580 182 2 12 156 278 369	10,233 10,157 9,359 6,095 2,179 835 296 2 9 138 270 325	10,699 11,404 9,950 6,317 2,375 966 319 1 11 122 271 281	9,214 10,476 9,222 6,031 2,288 973 295 3 17 157 268 261	9,458 10,505 8,850 5,895 2,426 1,007 320 1 205 382 313	8,322 9,001 7,715 5,320 2,264 897 277 2 277 2 27 17 225 384 304	8,010 8,248 7,053 4,990 2,139 892 288 1 1 6 259 368 289	6,798 7,165 6,118 4,483 1,958 829 280 0 18 311 421 290	5,525 5,617 4,654 3,631 1,613 730 242 0 242 0 26 306 374 249	8,493 8,956 7,881 5,292 2,102 857 278 1 16 209 335 298
Male	$\begin{array}{c} 20-29\\ 30-39\\ 40-49\\ 50-59\\ 60-69\\ 70-79\\ \geq 80\\ 0-9\\ 10-19\\ 20-29\\ 30-39\\ 40-49\\ 50-59\end{array}$	8,175 8,029 8,004 4,862 1,678 580 182 2 12 156 278 369 321	10,233 10,157 9,359 6,095 2,179 835 296 2 2 9 138 270 325 292	10,699 11,404 9,950 6,317 2,375 966 319 1 11 122 271 281 237	9,214 10,476 9,222 6,031 2,288 973 295 3 295 3 17 157 268 261 222	9,458 10,505 8,850 5,895 2,426 1,007 320 1 205 382 313 242	8,322 9,001 7,715 5,320 2,264 897 277 277 277 277 277 225 384 304 235	8,010 8,248 7,053 4,990 2,139 892 288 1 16 259 368 289 228	6,798 7,165 6,118 4,483 1,958 829 280 0 18 311 421 290 240	5,525 5,617 4,654 3,631 1,613 730 242 0 242 0 242 0 26 306 374 249 187	8,493 8,956 7,881 5,292 2,102 857 278 1 1 6 209 335 298 245

^aAdjusted infection rate (cases/1,000,000).

women and men in the 30-39 age group had the highest crude rate (8,956 and 335, respectively). Women tended to have a higher crude rate, but it peaked around 2014, and continued to decrease steadily. On the other hand, the 30-39 age group in men showed a peak around 2017 but remained high, or in the case of 40-49 age group, a stationary crude rate was observed (Table 2).

Purely spatial analysis of clusters

Jeollabuk-do was the most likely cluster (MLC) with relative risk (RR) and log likelihood ratio (LLR) of 1.70 and 7895.184 for the total study period. The joint cluster of Busan/Gyeongsangnam-do/Ulsan/Daegu was next (RR=1.27, LLR=5,771. 405), followed by Jeju-do (RR=1.86, LLR=4,159.725), Seoul (RR=1.19, LLR=2,998.914) and Gwangju (RR=1.12, LLR= 221.612). Urban and rural differences were prominent. Most major metropolitan areas except for Daejon and Sejong were clusters at some point during the study period. In contrast, only Jeollabuk-do and Gyeongsangnam-do were significant clusters among the provinces (Table 3; Fig. 1). Major cities (Seoul, Daegu, Busan, Gwangju), Jeju-do and Jeollabuk-do were significant clusters at the first tertile of 2012-2014. During the second tertile of 2015-2017, Gyeongsangnam-do and Ulsan became significant clusters, while Seoul became not significant. On the third tertile, Incheon became a significant joint cluster together with Seoul. Gyeongsangnamdo, Busan and Ulsan were not further significant. Seen altogether, the southern regions seem to be significant clusters.

Spatial variation in temporal trends analysis

Temporal trends analysis for the whole study period showed that trichomoniasis rate was decreasing in most clusters. Incheon was the only cluster with increasing rate (0.72%, LLR=740.745). Chungcheongbuk-do/Sejong/Daejeon joint cluster (-8.83%, LLR=305.845) showed the greatest decrease. Gangwon-do/Gwangju/Seoul joint cluster (-7.34%, LLR=852.650), Ulsan (-0.0024%, LLR=289.338), Gyeonggi-do (-3.73%, LLR=216.829) and Jeollabuk-do (-2.52%, LLR=168.491) all showed significant decreases (Table 4; Fig. 2).

Table 3. Regional clusters for T. vaginalis infection	from 2012 to 2020
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	District	Cases	Expected	Relative risk	Log likelihood ratio ^a	P-value
2012-2014	Seoul	111,411	86,718	1.38	4113.443	< 0.001
	Jeollabuk-do	24,531	16,008	1.56	2034.825	< 0.001
	Jeju-do	9,676	5,093	1.92	1651.701	< 0.001
	Daegu	28,999	21,371	1.38	1293.497	< 0.001
	Busan	35,528	30,162	1.19	486.738	< 0.001
	Gwangju	16,134	12,588	1.29	472.969	< 0.001
2015-2017	Busan, Gyeongsangnam-do, Ulsan, Daegu	114,997	87,094	1.44	5231.682	< 0.001
	Busan	42,020	28,928	1.50	2812.724	< 0.001
	Jeollabuk-do	25,304	15,422	1.68	2766.880	< 0.001
	Daegu	30,697	20,555	1.53	2296.591	< 0.001
	Jeju-do	8,655	5,306	1.64	898.886	< 0.001
	Ulsan	12,568	9,686	1.31	401.646	< 0.001
	Gyeongsangnam-do	29,712	27,925	1.07	59.983	< 0.001
	Gwangju	13,360	12,160	1.10	59.131	< 0.001
2018-2020	Jeollabuk-do	20,204	11,009	1.89	3213.317	< 0.001
	Jeju-do	8,406	4,055	2.10	1808.039	< 0.001
	Daegu	20,660	14,754	1.43	1108.866	< 0.001
	Incheon, Seoul	87,107	76,650	1.19	917.320	< 0.001
	Seoul	66,656	58,804	1.17	624.663	< 0.001
	Incheon	20,451	17,846	1.16	193.043	< 0.001
Total period	Jeollabuk-do	70,039	42,337	1.70	7895.184	< 0.001
	Busan, Gyeongsangnam-do, Ulsan, Daegu	287,305	239,295	1.27	5771.405	< 0.001
	Jeju-do	26,737	14,533	1.86	4159.725	< 0.001
	Seoul	260,892	227,134	1.19	2998.914	< 0.001
	Gwangju	37,281	33,504	1.12	211.612	< 0.001

^aClusters are shown in decreasing order of log likelihood ratio.

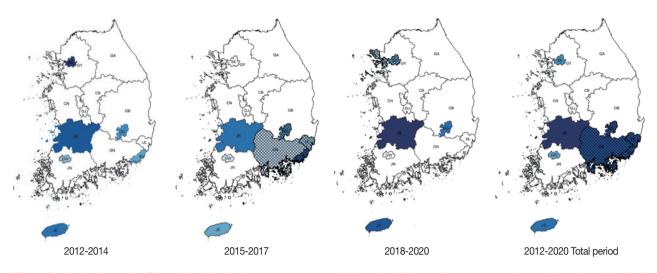


Fig. 1. Regional clusters for *T. vaginalis* infection from 2012 to 2020. Light to dark blue gradient represents increasing order of log likelihood ratio. Lattice patterns represent a joint cluster. Area codes represent administrative districts of the Korean government. SE, Seoul; BU, Busan; IN, Incheon; DG, Daegu; GW, Gwangju; DJ, Daejeon; UL, Ulsan; GY, Gyeonggi-do; GA, Gangwon-do; CB, Chungcheong-buk-do; CN, Chungcheongnam-do; JB, Jeollabuk-do; JN, Jeollanam-do; GB, Gyeongsangbuk-do; GN, Gyeongsangnam-do; JE, Jeju-do; SJ, Sejong.

Table 4. Spatiotemporal trends analysis of trichomoniasis according to administrative districts (2012-2020)

Districts	Cases	Expected	Trend inside clusterª	Trend outside cluster ^a	Relative risk	Log likelihood ratio ^b	P-value
Gangwon-do, Gwangju, Seoul	317,171	295,956	-7.34	-4.18	1.10	852.650	< 0.001
Incheon	60,760	66,805	0.72	-5.36	0.90	740.745	< 0.001
Chungcheongbuk-do, Sejong, Daejeon	54,060	76,151	-8.83	-4.86	0.70	305.845	< 0.001
Ulsan	31,765	26,471	0.00°	-5.19	1.21	289.338	< 0.001
Gyeonggi-do	270,493	290,982	-3.73	-5.42	0.91	216.829	< 0.001
Jeollabuk-do	70,039	42,337	-2.52	-5.19	1.70	168.491	< 0.001

^aTrend inside/outside cluster denotes % increase/decrease over the period of 2012-2020.

^bClusters are shown in decreasing order of log likelihood ratio.

°Real value: -0.0024.

Trends of trichomoniasis in age groups according to sex

Changes in crude rate of women and men are shown in Fig. 3. In women, the 20-59 age groups showed sharp increasing rates until 2014 (trend 1) but were not significant. From 2014 on, they showed significant decrease (trend 2). The 60-69 age group showed a more gradual rise and decrease, which was significant at trend 2. The 70-79 age group showed an even more gradual change, but it was significant throughout the whole period. Overall, trichomoniasis seems to be decreasing in women currently after peaking around 2014 (Fig. 3A). Although the crude rate is far smaller than that of women, men showed different trends according to age. The 10-39 age groups showed significant increasing rates throughout the study period. In contrast, the 40-59 age groups showed significant decrease during the same period (Fig. 3B).

A joinpoint was observed in all female age groups of 10-19 and older, although the increasing first trend was not significant except for the 70-79 age group (31%, P = 0.026). The first trend was seen mostly during 2012-2014. *Trichomonas* infection decreased significantly during the second trend, which was mostly 2014-2020, in most age groups (all P < 0.05), except for the 10-19 and ≥ 80 age groups (P = 0.053 and 0.050, respectively). On the other hand, no joinpoint was observed in the male age groups. The 10-19, 20-29, and 30-39 age groups showed a significant increase while the 40-49 and 50-59 age groups showed significant decrease. Although not significant, increasing rates were observed in the 60-69 and older age groups (Table 5).

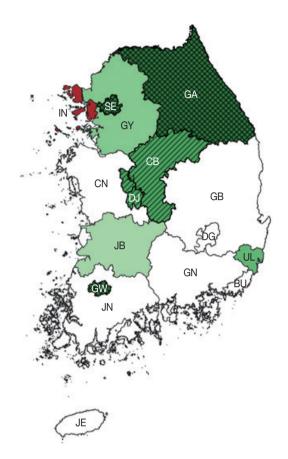


Fig. 2. Spatiotemporal trend analysis of trichomoniasis according to districts. Green and red indicate decreasing and increasing rate of infection within the cluster, respectively. Light to dark green gradient represents increasing order of log likelihood ratio. Lattice patterns and dashed lines represent joint clusters in decreasing order of log likelihood ratio. Area codes represent administrative districts of the Korean government. SE, Seoul; BU, Busan; IN, Incheon; DG, Daegu; GW, Gwangju; DJ, Daejeon; UL, Ulsan; GY, Gyeonggi-do; GA, Gangwon-do; CB, Chungcheongbuk-do; CN, Chungcheongnam-do; JB, Jeollabuk-do; JN, Jeollanam-do; GB, Gyeongsangbuk-do; GN, Gyeongsangnam-do; JE, Jeju-do; SJ, Sejong.

DISCUSSION

The present study provides an overview of the latest *Trichomonas* infection status in Korea by determining trichomoniasis clusters and evaluating temporal trends according to districts and age or sex during 2012-2020.

The incidence and prevalence of trichomoniasis are known to be varied depending on the population, time, and region, but they are higher in women and older age groups compared to men or younger age groups [24]. Joo et al. [25] have reported that trichomoniasis emerged as the most common non-viral sexually transmitted diseases (STD) among the total population during 2009-2014. Some overlap occurs, but in the current study, we strived to further analyze more recent data statistically.

Gyeonggi-do had the highest average number of cases, not surprising as this province also has the highest average population. Busan had the highest average crude rate after adjusting for the population. Busan is one of the major metropolitan cities in Korea, and major cities tended to have a higher crude rate compared to the provinces.

The 40-49 and 30-39 age groups in women showed the highest average cases of trichomoniasis, and this was also observed in the same age groups of men. After adjusting for the population, both women and men in the 30-39 age group had the highest crude rate. These findings were consistent with that reported by Joo et al. [25]. Women tended to have a higher crude rate, but it peaked around 2014 and decreased steadily. On the other hand, the 30-39 age group in men showed a peak around 2017 but remained high, or in the case of 40-49 age group, a stationary crude rate was observed.

Most major metropolitan areas were clusters at some point during the study period. This might have been caused by urban and rural differences, as a high population density or ready access to health resources in major cities seems to be the most probable cause.

Jeollabuk-do and Gyeongsangnam-do were clusters among the provinces. To our surprise, Jeollabuk-do was the most likely cluster for the whole study period, and this was a finding also noted by Joo et al. [25]. They have reported this finding for 2009-2014, so trichomoniasis is still prevalent for over a decade. The cause is still unclear. Although Gyeongsangnamdo is a province, it is near or borders the major cities of Busan, Ulsan, and Daegu. This might have caused in it becoming a joint cluster. The southern regions seem to be significant clusters. Jeju-do is a province but being a semi-tropical island in the southern region, it is a favorite travelling destination. A large influx of outsiders may have caused in it being a cluster.

Trichomoniasis was decreasing in most clusters, except for Incheon. Incheon is a major metropolitan city and has several characteristics that might have had an influence in the outcome. Besides having a large population and industry itself, it also has a major seaport and airport that serves as a major transition point for adjacent Seoul and Gyeonggi-do, the largest city and province, respectively, in terms of population. A large number of people living in Incheon commutes to the surrounding areas. It also has many islands, which means lim-

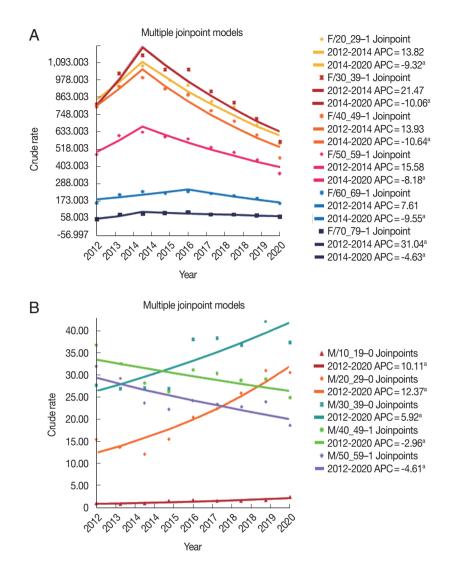


Fig. 3. Trend analysis of trichomoniasis according to sex. (A) In women, the 20-59 age groups show sharp increasing rates until 2014 (trend 1), but are not significant. From 2014 on, they show significant decrease (trend 2). Annual Percentage Changes (APC) for the 20-29, 30-39, 40-49, and 50-59 age groups are –9.3, –10.1, –10.6, and –8.2, respectively. The 60-69 age group shows a more gradual rise and decrease (significant trend 2) with APC –9.6. The 70-79 age group shows an even more gradual change, but is significant throughout the whole period, with APC 31.0 and –4.6 in trend 1 and 2, respectively. (B) In men, the 10-39 age groups show significant increasing rates throughout the study period. APC for the 10-19, 20-29, and 30-39 age groups are 10.1, 12.4, and 5.9, respectively. In contrast, the 40-59 age groups show significant decrease during the same period. APC for 40-49 and 50-59 age groups are –3.0 and –4.6, respectively. Only significant trends are shown. Crude rates (adjusted cases per 100,000 population at risk) are calculated by mid-year in Joinpoint, so the program outputs 2014 (B) and 2018 (A) twice on the X axis to reflect multiple trends. alndicates that the APC is significant at the alpha=0.05 level.

ited health resources spread thinly over a vast area.

Chungcheongbuk-do/Sejong/Daejeon joint cluster showed the greatest decrease. Although Daejon is a major city, its nearby Chungcheongbuk-do has a low population compared to the other provinces. Sejong is a fairly new city that was only inaugurated in 2012. It is also a specialized city with mainly public and administrative organizations, so besides its size, its population composition tends to be different from other cities. These factors may have contributed to the significant decrease in trichomoniasis. A low population density might also have had an influence in Gwangwon-do. It was also decreasing in most metropolitan cities. Increased awareness of the disease and introduction of more sensitive diagnostic tests might have had an influence, as initially the incidence had risen around 2014, and then decreased steadily [25].

Trichomoniasis cases increased in most female age groups

	Ago group		Tre	nd 1		Trend 2				
	Age group	Period	APC ^a	95% CI	P-value	Period	APC ^a	95% Cl	P-value	
Female	0-9	2012-2020	-3.6	-9.7~2.8	0.22					
	10-19	2012-2014	15.5	-17.1~60.8	0.29	2014-2020	-6.0	-11.8~0.1	0.05	
	20-29	2012-2014	13.8	-13.9~50.4	0.27	2014-2020	-9.3	-13.9~-4.5	0.01	
	30-39	2012-2014	21.5	-5.2~55.7	0.10	2014-2020	-10.1	-14.2~-5.7	0.00	
	40-49	2012-2014	13.9	-9.5~43.5	0.19	2014-2020	-10.6	-14.5~-6.5	0.00	
	50-59	2012-2014	15.6	-6.6~43.0	0.13	2014-2020	-8.2	-11.5~-4.7	0.00	
	60-69	2012-2016	7.6	-3.3~19.7	0.13	2016-2020	-9.6	-17.7~-0.6	0.04	
	70-79	2012-2014	31.0	5.6~62.7	0.03	2014-2020	-4.6	-7.5~-1.6	0.01	
	≥80	2012-2014	27.2	-8.8~77.4	0.12	2014-2020	-4.2	-8.2~0.0	0.05	
Male	0-9	2012-2020	-9.9	-26.4~10.4	0.26					
	10-19	2012-2020	10.1	3.3~17.3	0.01					
	20-29	2012-2020	12.4	8.2~16.7	0.00					
	30-39	2012-2020	5.9	2.5~9.5	0.00					
	40-49	2012-2020	-3.0	-5.7~-0.2	0.04					
	50-59	2012-2020	-4.6	-7.4~-1.8	0.01					
	60-69	2012-2020	0.2	-3.2~3.7	0.90					
	70-79	2012-2020	1.5	-3.0~6.3	0.46					
	≥80	2012-2020	3.4	-6.2~14.0	0.45					

Table 5. Trichomoniasis trends according to sex and age

^aAPC: annual percentage change.

during 2012-2014 but were not significant except for the elderly (70-79 age group). Kim et al. [26] have reported a similar finding in a previous study. However, after around 2014, trichomoniasis decreased significantly in nearly all age groups. The Special Law on Sex Trade was enacted in September 2004. Prostitution has always been illegal in Korea, but up to then the authorities had turned a blind eye to it. Since then, prohibition was strictly implemented, and it might also have had an influence.

Trichomoniasis in the male age groups revealed a different trend. The 40-49 and 50-59 age groups showed significant decrease, but in comparison to the same age group in women, the decrease was progressively linear. The decrease might be explained like in women above. On the other hand, a marked age demarcation was noted around the age of 40. It showed a significantly progressive increasing trend in the age groups below 40. According to a 2012 study by the Ministry of Gender Equality and Family, runaway youths, that included at-risk youths and same age group students, have been exposed to various sex-related problems. At-risk youths, compared to their counterpart students, experienced 3 times more prostitution (11.0% vs. 3.3%). Sexual relationship was even higher, at-risk vouths experiencing 6 times more than the comparable students (36.3% vs. 5.6%) [http://www.mogef.go.kr/mp/pcd/ mp_pcd_s001d.do;jsessionid = fqV5nBCWAC9phOl6rwJ- kN5h.mogef20?mid = plc502&bbtSn = 691646]. Unfortunately, rapid changes in society might aggravate this kind of problem further, and it might also have an impact on future trends of the infection.

In conclusion, our study was able to recognize the current status and trend of trichomoniasis in Korea, augmenting the study by Joo et al. [25]. This study might provide an analytic basis for future health measures and help policy-makers and health authorities in developing effective system for prevention of trichomoniasis.

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CONFLICT OF INTEREST

The authors declare no conflict of interest related to this study.

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