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ORIGINAL ARTICLE

Cluster of Parasite Infections by the Spatial Scan Analysis in Korea

Kyoung-Eun Bae[1], Yoon Kyung Chang[2], Tong-Soo Kim[3], Sung-Jong Hong[4], Hye-Jin Ahn[2], Ho-Woo Nam[2], Dongjae Kim[1,*]

[1]Department of Biomedicine Health Science, College of Medicine, The Catholic University of Korea, Seoul 06591, Korea; [2]Department of Parasitology, College of Medicine, The Catholic University of Korea, Seoul 06591, Korea; [3]Department of Parasitology and Tropical Medicine and Inha Research Institute for Medical Sciences, Inha University School of Medicine, Incheon 22333, Korea; [4]Department of Medical Environmental Biology, Chung-Ang University College of Medicine, Seoul 06974, Korea

Abstract: This study was performed to find out the clusters with high parasite infection risk to discuss the geographical pattern. Clusters were detected using SatScan software, which is a statistical spatial scan program using Kulldorff's scan statistic. Information on the parasitic infection cases in Korea 2011-2019 were collected from the Korea Centers for Disease Control and Prevention. Clusters of *Ascaris lumbricoides* infection were detected in Jeollabuk-do, and *T. trichiura* in Ulsan, Busan, and Gyeongsangnam-do. *C. sinensis* clusters were detected in Ulsan, Daegu, Busan, Gyeongsangnam-do, and Gyeongsangbuk-do. Clusters of intestinal trematodes were detected in Ulsan, Busan, and Gyeongsangnam-do. *P. westermani* cluster was found in Jeollabuk-do. *E. vermicularis* clusters were distributed in Gangwon-do, Jeju-do, Daegu, Daejeon, and Gwangju. This clustering information can be referred for surveillance and control on the parasitic infection outbreak in the infection-prone areas.

Key words: *Ascaris lumbricoides*, *Trichuris trichiura*, cluster, Korea

INTRODUCTION

Parasitic infection rate in Republic of Korea has decreased ever since the national public health project (the Parasite Disease Prevention Act) took effect in 1966. According to National Survey on Parasitic Infection, which has been conducted every 5-7 years, the overall helminth egg positive rate was 2.6% in the 8th survey, decreased from 2.7% of the 7th survey, yet the estimated number of infections nationwide was about 1.3 million [1,2]. According to the 8th survey, the parasite of the highest infection rate was *Clonorchis sinensis* with the rate of 1.9%, which took 70% from the total infection. This was a significant implication for parasite prevalence, meaning that parasite epidemic has been changed from soil-borne such as *Ascaris lumbricoides* and *Trichuris trichiura* to fish–borne infections [2]. In addition, there are still a significant number of cases of parasitic infection reported every year and complications of these infections can develop into serious diseases. Therefore, it is necessary to find a cluster where infection risk is significantly high and discuss the prevalence pattern to monitor and prevent the parasite infection in susceptible areas. To detect a cluster, Kulldorff's SaTScan Software was used, which provides computational resource that enables researchers to locate and statistically test the clusters [3].

MATERIALS AND METHODS

Ethics statement

This study was performed under the regulation of the IRB Committee of The Catholic University of Korea (No. MIRB-20200529-002). This research adhered to the tenets of the Declaration of Helsinki.

Data Source and definition

The nationwide parasitic infection cases reported for 9 years (2011-2019) were collected from 16 administrative districts by the Korea Disease Control and Prevention Agency (KCDA) [4]. The parasitic infections were of *Ascaris lumbricoides*, *Trichuris trichiura*, *Clonorchis sinensis*, *Paragonimus westermani*, intestinal trematodes and *Enterobius vermicularis*.

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* Corresponding author (djkim@catholic.ac.kr)

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The population data of 16 administrative divisions 2011-2019 were obtained from the Korean Statistical Information Service [5]. The geographical locations of the infection 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 parasitic infection cases were summed up as accumulated counts and numbers for the 9 years by administrative district (Table 1).

Spatial scan statistical analyses

SaTScan Software using the spatial scan statistic [3] were employed to cluster the parasitic infection cases and to evaluate statistical significance of the located clusters through simulation. The discrete Poisson model was used since the parasitic infection case data were linked to their background population at risk [6]. The spatial scan statistic detected clusters by creating a circular window on a map and scanning the study area by varying a window size. The null hypothesis is that disease risk of both inside and outside of the window are the same, while the alternative hypothesis is that disease risk within the window is different from the outside [7]. A likelihood ratio for every window was calculated and the maximum likelihood ratio was defined as the test statistic. The window with the maximum likelihood ratio was identified as the most likely cluster, the significant cluster which is least likely to have occurred by chance while other windows were classified as secondary clusters. The window size determines a percentage of the population at risk within the window and SaTscan Software provides its users an option to set maximum cluster size, the upper bound of window size. [6,8]. By increasing window size, its radius expands until the risk population within the window reaches the set value. If other administrative districts are located within the radius, the cluster is created by combining 2 districts into one and becomes larger cluster [7]. Therefore, increase of the window size resulted in larger clusters by merging of adjacent administrative districts in the radius [7,9]. It is important to find appropriate set value of cluster size because large value could hide effect of small core clusters, and small value could overlook the regional pattern of clusters [10]. This study adapted 5%, 15%, and 25% as the values to spot the cluster in different window size. Statistical significance of the clusters was calculated using the Monte Carlo simulations [11,12] and expressed as p-value. A significance level of alpha <0.05 was used as a standard. R program (ver. 4.0.1) was used to visualize cluster patterns on a map. The clusters were numbered in order of likelihood ratio. This study analyzed accumulated data for 9 years, 2011-2019, without taking time into account.

RESULTS

General clustering

With 5% maximum cluster size, Ulsan, Daegu, Jeju-do, and

Table 1. The cumulated parasite infection cases and population for 2011-2019 by administrative district

District (no.)	Population	No. of infection cases of					
		Ascaris lumbricoides	*Trichuris trichiura*	*Clonorchis sinensis*	Intestinal trematodes	*Paragonimus westermani*	*Enterobius vermicularis*
Seoul (1)	89,996,828	17	158	421	59	6	185
Busan (2)	31,474,736	3	514	5,265	898	0	11
Daegu (3)	22,355,184	1	114	1,849	178	1	226
Incheon (4)	26,156,739	6	41	87	5	0	10
Gwangju (5)	13,202,461	1	17	479	33	1	121
Daejeon (6)	13,604,984	9	92	227	27	0	134
Ulsan (7)	10,420,219	0	93	2,739	169	0	63
Gyeonggi-do (8)	113,053,274	4	152	279	60	2	192
Gangwon-do (9)	13,896,792	1	5	16	2	0	788
Chungcheongbuk-do (10)	14,249,464	0	6	217	28	0	10
Chungcheongnam-do (11)	18,781,102	0	0	0	0	0	8
Jeollabuk-do (12)	16,736,755	15	32	188	44	7	47
Jeollanam-do (13)	17,097,958	0	0	20	0	0	2
Gyeongsangbuk-do (14)	24,235,379	0	0	146	52	0	0
Gyeongsangnam-do (15)	30,167,674	4	538	4,728	1,988	1	24
Jeju-do (16)	5,622,276	0	0	3	1	0	551
Total	461,051,825	61	1,762	16,664	3,544	18	2,372

Gangwon-do were clustered. Ulsan was the most likely cluster (LLR) with relative risk (RR) of 6.2, indicating that total parasite infection risk in Ulsan was 6.2 times higher than in the other districts. Followed were Daegu, Jeju-do and Gangwon-do in order of their likelihood ratio. With 15% maximum window size, Busan and Gyeongsangnam-do was the most likely cluster, indicating parasitic infection risk in Busan and Gyeongsangnam-do area was 8.7 times higher than other areas. With 25% maximum window size, Busan, Gyeongsangnam-do, Ulsan and Daegu were the most likely cluster, indicating the total parasite infection risk in these districts was 15 times higher than in the other districts (Table 2). The general parasitic infection 2011-2019 showed that core outbreaks were prominent in Ulsan, Daegu, and Jeju-do while the regional outbreak pattern was found in the southeastern region such as Busan, Gyeongsangnam-do, Ulsan, and Daegu (Fig. 1).

Clusters of *Ascaris lumbricoides* and *Trichuris trichiura*

With 5% maximum cluster size, the cases of *A. lumbricoides* were most likely cluster in Jeollabuk-do, indicating the risk of *A. lumbricoides* infection was 8.7 times higher in Jeollabuk-do than other areas. The secondary cluster was Daejeon. With 15% of maximum cluster size, the most likely cluster was Jeollabuk-do and Daejeon. Clustering with 25% window was same to that of 15%. The cases of *A. lumbricoides* infection were mainly distributed in Jeollabuk-do.

T. trichiura with 5% maximum cluster size, the most likely cluster was Ulsan with relative risk of 2.4 while secondary clusters were Daejeon and Daegu. With 15% maximum cluster size, Busan and Gyeongsangnam-do was the most likely cluster with relative risk of 9.6, indicating *T. trichiura* infection risk was 9.6 times higher in Busan and Gyeongsangnam-do. The secondary cluster was Daejeon. With 25% maximum cluster size, Busan, Gyeongsangnam-do and Ulsan was the most like-

Table 2. Clusters detected from general parasite infection by window size

Window Size	District	Case No.	Relative risk	Log likelihood ratio	*P*-value
5%	Ulsan	3,064	6.2	2,876.845	<0.001
	Daegu	2,369	2.11	488.693	<0.001
	Jeju-do	555	1.88	89.688	<0.001
	Gangwon-do	812	1.11	3.908	0.024
15%	Busan, Gyeongsangnam-do	13,974	8.67	12,945.557	<0.001
	Jeju-do	555	1.88	89.688	<0.001
25%	Busan, Gyeongsangnam-do, Ulsan, Daegu	19,407	15.03	19,526.059	<0.001

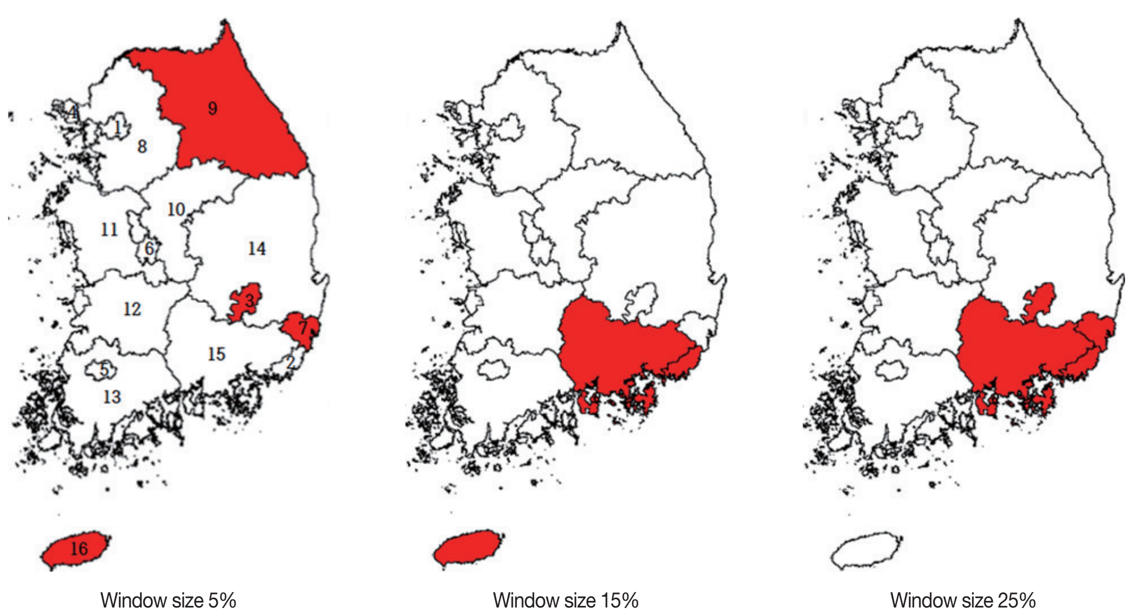

Fig. 1. Clusters detected in general parasitic infections by window size. Numbers identifying the administrative districts are referred to Table 1.

Table 3. Clusters detected from *Ascaris lumbricoides* and *Trichuris trichiura* infections by window size

Window size	District	Case No.	Relative risk	Log likelihood ratio	*P*-value
Ascaris lumbricoides					
5%	Jeollabuk-do	15	8.66	17.414	<0.001
	Daejeon	9	5.69	7.742	<0.001
15%	Jeollabuk-do, Daejeon	24	9.21	26.936	<0.001
25%	Jeollabuk-do, Daejeon	24	9.21	26.936	<0.001
Trichuris trichiura					
5%	Ulsan	93	2.41	26.531	<0.001
	Daejeon	92	1.81	12.966	<0.001
	Daegu	114	1.36	4.562	0.011
15%	Busan, Gyeongsangnam-do	1,052	9.6	1,030.771	<0.001
	Daejeon	92	1.81	12.966	<0.001
25%	Busan, Gyeongsangnam-do, Ulsan	1,145	10.02	1,088.969	<0.001
	Daejeon	92	1.81	12.966	<0.001

Table 4. Clusters detected from *Clonorchis sinensis*, intestinal trematodes and *Paragonimus westermani* by window size

Window size	District	Case No.	Relative risk	Log likelihood ratio	*P*-value
Clonorchis sinensis					
5%	Ulsan	2,739	8.51	3252.351	<0.001
	Daegu	1,849	2.45	524.628	<0.001
15%	Busan, Gyeongsangnam-do	9,993	9.71	9847.711	<0.001
	Gyeongsangbuk-do, Daegu	1,995	1.21	30.359	<0.001
25%	Busan, Gyeongsangnam-do, Ulsan, Daegu	14,581	27.18	17321.082	<0.001
Intestinal trematodes					
5%	Ulsan	169	2.17	38.432	<0.001
15%	Busan, Gyeongsangnam-do	2,886	28.42	4200.849	<0.001
25%	Busan, Gyeongsangnam-do, Ulsan	3,055	33.72	4330.98	<0.001
Paragonimimus westermani					
5%	Jeollabuk-do	7	16.89	11.5896	<0.001
15%	Jeollabuk-do	7	16.89	11.5896	<0.001
25%	Jeollabuk-do	7	16.89	11.5896	<0.001

ly cluster with relative risk of 10, indicating *T. trichiura* infection in Busan, Gyeongsangnam-do and Ulsan area was 10 times higher than other regions (Table 3). Overall, 15% and 25% analysis showed that big clusters including Busan and Gyeongsangnam-do region had notably high risk of indicating *T. trichiura* infection.

Clusters of *Clonorchis sinensis*, intestinal trematodes and *Paragonimus westermani*

C. sinensis with 5% maximum cluster size, Ulsan was the most likely cluster with relative risk of 8.5, indicating *C. sinensis* infection in Ulsan was 8.5 times higher than other areas. The secondary cluster was Daegu. With 15% maximum cluster size, Busan and Gyeongsangnam-do was the most likely cluster with relative risk of 9.7. Gyeongsangbuk-do and Daegu was the secondary cluster. With 25% maximum cluster size, Busan, Gyeongsangnam-do, Ulsan and Daegu were the most likely cluster with relative risk of 27.2. Spatial scan analysis on the *C. sinensis*-infected cases showed a consistent pattern in every cluster size that the *C. sinensis* infection risk was prominent in Gyeongsangnam-do (Table 4).

For intestinal trematodes, with 5% maximum cluster size, the most likely cluster was Ulsan with relative risk of 2.2, indicating that the intestinal trematode infections in Ulsan was 2.2 times higher than in the other areas. With 15% maximum cluster size, the most likely cluster was Busan and Gyeongsangnam-do with relative risk of 28.4. With 25% maximum cluster size, the most likely cluster was Busan, Gyeongsangnam-do and Ulsan with relative risk of 33.7. In summary, the intestinal trematode infection was of high risk in Gyeongsangnam-do region.

The clusters of *P. westermani* infections with 5%, 15%, and

Table 5. Clusters detected from *Enterobius vermicularis* infection by window size

Window size	District	Case No.	Relative risk	Log likelihood ratio	*P*-value
5%	Gangwon-do	788	16.01	1,299.982	<0.001
	Jeju-do	551	24.51	1,164.773	<0.001
	Daegu	226	2.07	44.449	<0.001
	Daejeon	134	1.97	23.916	<0.001
	Gwangju	121	1.82	17.406	<0.001
15%	Gangwon-do	788	16.01	1,299.982	<0.001
	Jeju-do	551	24.51	1,164.773	<0.001
	Daegu	226	2.07	44.449	<0.001
	Daejeon	134	1.97	23.916	<0.001
	Gwangju	121	1.82	17.406	<0.001
25%	Gangwon-do	788	16.01	1,299.982	<0.001
	Jeju-do	551	24.51	1,164.773	<0.001
	Daegu	226	2.07	44.449	<0.001
	Daejeon	134	1.97	23.916	<0.001
	Gwangju	121	1.82	17.406	<0.001

25% window size were all same. The most likely cluster was in Jeollabuk-do with relative risk of 16.9.

Clusters of *Enterobius vermicularis*

With 5% maximum cluster size, Gangwon-do was the most likely cluster with relative risk of 16, indicating *E. vermicularis* infection risk in Gangwon-do was 16 times higher than in the other regions. The secondary cluster was in Jeju-do followed by Daegu, Daejeon and Gwangju. Jeju-do, however, showed exceptionally relative risk of 24.51 (Table 5). In *E. vermicularis* infection analysis, the results of 15% and 25% windows were the same to that of 5% window. The *E. vermicularis* infections distributed all over the study regions, while Gangwon-do and Jeju-do showed high risk of enterobiasis.

DISCUSSION

This study has provided the clusters with high risk of parasitic infection in Korea from 2011 to 2019, by using spatial scan analysis. Depending on the transmission of infections, the infections are respectively divided into soil-borne, fish-borne, and contact-borne.

A. lumbricoides and *T. trichiura* are soil-transmitted helminths by ingesting worm eggs in the soil. According to Nationwide Survey on the Prevalence of Intestinal Parasitic Infections, *A. lumbricoides* showed a dramatic decrease of egg positive rate from 54.9% in the 1st survey in 1971 to 0.03% in the 8th survey in 2012 and *T. trichiura* from 65.4% to 0.4% [13]. The tendency of decrease also showed in this study that the soil-transmitted helminths infection cases comprised 7.5% of the data and especially with 61 reported *A. lumbricoides* cases nationwide in 9 years (Table 1). *A. lumbricoides* clusters were located in the southern-west and *T. trichiura* clusters, mostly in southern-east. The most *T. trichiura* infection-prone area consisted of Busan, Gyeongsangnam-do, Ulsan. Daejeon was also infection-prone area for *A. lumbricoides* and *T. trichiura* by being an overlapping cluster of both infections. The successful control over soil-transmitted helminths was carried out as economic growth of Korean society brought improvement of sanitary condition. Also, the use of chemical fertilizers on farm brought the change since traditional agricultural industry in 1970s used human manure as a fertilizer causing the widespread worm eggs in the soil and agricultural products growing on it [13].

C. sinensis, intestinal trematodes, and *P. westermani* are the fish-borne parasites transmitted by ingesting undercooked fresh-water fish and shellfish. The geographical locations of *C. sinensis* and intestinal trematodes infection-prone area was southern-east region including Busan, Gyeongsangnam-do, Ulsan while *P. westermani* was located in Jeollabuk-do (Fig. 2). The 3 fish-borne parasites consisted about 83% of the reported case data showing the prevalence of consuming raw or undercooked food. This culinary tradition came from the previous generation who had fresh-water fish and shellfish as a source of protein during famine. In addition, the tradition remains and is enjoyed by people in all generation. Therefore, reported cases could be infections from both past and present. The 7th survey in 2004 showed that fish-borne parasitic infection was steadily prevalent along the riverside areas [13].

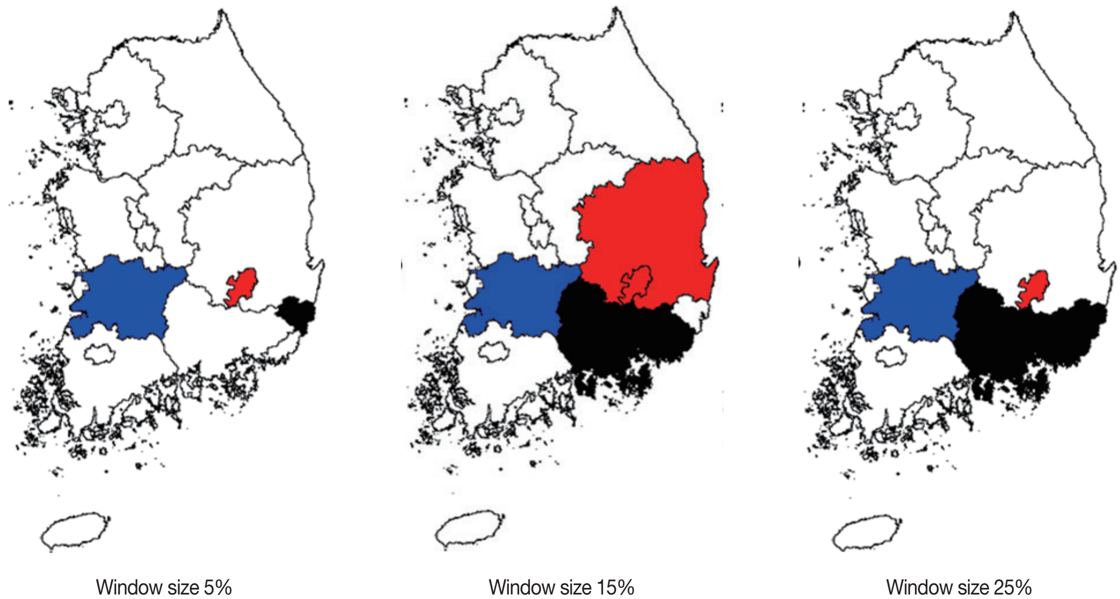

Fig. 2. Clusters detected from *Clonorchis sinensis* (red), intestinal trematodes, and *Paragonimus westermani* (blue) infections by window size. Clusters overlapped with *C. sinensis* and intestinal trematode infections are colored black.

E. vermicularis, also known as the pinworm, is transmitted by physical contact. The geographical clusters of Enterobius vermicularis were distributed all over the region. It is the common infection among preschool or school-age children and since the government is expanding the pre-school education, it is more likely to be increased [1].

CONFLICT OF INTEREST

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

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