

Seropositivity Rates of *Strongyloides stercoralis* Antibody in the Southeastern Region of Republic of Korea: A Single-Center Retrospective Study

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Abstract: *Strongyloides stercoralis* infection is not endemic in the Republic of Korea (Korea) with a positivity rate of < 1% in stool examination. However, there is a risk of hyperinfection in immunosuppressed individuals. It is necessary to determine the seropositivity of *S. stercoralis* antibodies in Korea. This study investigated the seropositivity of *S. stercoralis* antibodies in the southeastern area of Korea. From January 2019 to June 2021, serum samples were collected from participants who visited the study center in the southeastern region of Korea for routine health check-ups. We determined serum levels of specific anti-*Strongyloides* IgG antibodies in 834 samples by enzyme-linked immunosorbent assay. We observed that 92 samples (11.0%) tested showed a positive response. The age of the participants was 51 ± 10.7 years, and 43.4% of them were men. The antibody positivity rate based on the location of the participants' residence were 12.3% (Gyongsangnam-do), 10.2% (Busan), and 10.1% (Ulsan), respectively. Total eosinophil count was associated with positive test results (154.8 ± 152.0 per mm^3 versus 202.1 ± 178.9 per mm^3 , $P=0.006$). Logistic regression analysis revealed that blood eosinophil count, age above 50 years, and residence in Sacheon were factors associated with the positive status of *S. stercoralis* antibody. Our finding suggests that it is necessary to test for *S. stercoralis* in actual clinical settings in Korea.

Key words: *Strongyloides stercoralis*, IgG antibody, seroprevalence, ELISA, Korea

INTRODUCTION

Strongyloides stercoralis is a parasite that causes enteric infections in animals and humans [1]. The infection is widespread in most tropical and subtropical regions, with prevalence rate exceeding 70% in some countries, such as Peru, Dominica, Kenya, and Ghana [2]. Moreover, the infection is distributed widely, affecting up to 370 million humans worldwide [2]. More than 50% of cases with strongyloidiasis are asymptomatic, and the remaining cases present mainly with gastrointestinal symptoms, including abdominal pain and chronic diarrhea [3]. However, in approximately 2.5% of cases, hyperinfection or disseminated infection that invades other organs occurs in immunocompromised patients, resulting in a serious

prognosis [4].

In the Republic of Korea (Korea), the first case of strongyloidiasis was reported in 1914, and approximately 35 cases have been reported in the literature [3,5-14]. However, the seroprevalence of *S. stercoralis* infection has not yet been investigated in Korea. The egg-positive rate of *S. stercoralis* in stool samples was reported to be less than 1% in a previous study [15]. The lack of serologic studies on *S. stercoralis* in Korea is because clinicians did not suspect this disease, and therefore, studies for serological diagnosis of *S. stercoralis* has seldom been conducted in Korea. However, a recent study reported that the prevalence of strongyloidiasis in Northeast Asia was estimated to be 5-10% [16]. The present study aimed to investigate the seropositivity of *S. stercoralis* in the southeastern area of Korea by detecting serum levels of specific anti-*Strongyloides* antibodies. Further, this study analyzed the difference of epidemiologic characteristic between the seropositive and seronegative groups.

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MATERIALS AND METHODS

Ethics statement

The present study had obtained ethical approval from the Institutional Review Board of Pusan National University Yangsan Hospital (approval no. 05-2021-296). Informed consent was obtained from all the participants.

Study design

This study was a retrospective cross-sectional study of a single center. In this study, samples were collected from people who visited the study center for health screening between January 2019 and June 2021. Testing for *S. stercoralis* antibody and data collection were performed retrospectively. The study excluded those who had a minimal serum sample volume or who refused to donate residual samples. Residual serum samples were collected from people who underwent blood tests for routine health screening. The specimens were stored by Human Material Bank of Pusan National University Yangsan Hospital. After centrifugation of the blood, the samples were stored at -40°C .

To determine the presence of IgG antibodies against *S. stercoralis*, we used *Strongyloides ratti* enzyme-linked immunosorbent assay (Bordier Affinity Products, Crissier, Switzerland). It has a specificity of 98.3% (95.9-100%) and a sensitivity of 89.5% (83.8-95.1%) [17]. We used the G power 3.1.9.2 program to calculate the required sample size. More than 64 participants were needed in each positive and negative group for using independent *t* test. Based on these findings, we decided to examine at least 640 specimens.

Study location and population

Korea has a latitude of 33° to 38° north and a longitude of 126° to 132° east. Gyeongsangnam-do (do=province), Busan, and Ulsan metropolitan city are located in the southeastern region of the Korean Peninsula. The central region has a continental dry winter climate (Dwa). By contrast, the southeastern region is a coastal region and has monsoon-influenced humid subtropical dry hot (Cwa), subtropical hot humid (Cfa), and Dwa climates (Supplementary Figs. S1, S2) [18]. The coastal area influences the area considerably because it is confined by high mountains to the north, which shut out the cool winter wind from the northwest. This creates the most moderate climate in Korea with an annual average temperature of $12-13^{\circ}\text{C}$, an annual precipitation level of 1,400-1,800 mm, and mean

temperatures of -0.5°C and 25.1°C in January and August, respectively. The population in this region was 7,868,179 in 2020, accounting for 15.1% of the total population of Korea [19,24]. The study center was Pusan National University Yangsan Hospital, which is located in Yangsan, Gyeongsangnam-do (Fig. 1). Owing to these regional characteristics, most of the visitors to the study center are residents of the southeastern part of Korea.

Statistical analysis

To analyze differences in age, sex, place of residence, and blood eosinophil count between the seropositive and seronegative groups, an independent *t*-test was used for continuous variables, and the chi-square test or Fisher's exact test were used for categorical variables. Age was analyzed using both methods with additional categorization. For variables showing a difference in the univariate analysis, a *P* value of <0.05 was included in the logistic regression model. All tests were 2-sided, with a significance level of 0.05. Data analysis was performed using IBM SPSS Statistics for Windows, version 27 (IBM Corp, Armonk, New York, USA).

RESULTS

A total of 834 specimens were tested in this study, and 92 of them were seropositive (11.0%) (Table 1). The positivity rate was significantly higher in men in the univariate analysis ($P=0.014$). There were no statistically significant differences in mean age between the groups ($P=0.200$). However, age >50 years was significantly associated with positive results ($P=0.036$). The eosinophil count and sex of the participants were significantly different between the positive and negative groups ($P=0.006$ and $P=0.014$, respectively). The positivity rate was $>10\%$ in 7 cities and rural areas, including Busan and Ulsan, which are metropolitan cities (Table 2; Fig. 1). In 1 city and 1 rural area, the positive rate was 50%, but the number of participants was small; therefore, caution is needed for interpretation. However, there was a statistically significant correlation between the positive test results and living in Sacheon ($P=0.020$). Since this study was conducted using donated specimens, the occupation of the subjects could not be identified. Using logistic regression analysis (Table 3), age >50 years (odds ratio (OR) = 1.674, 95% confidence interval (CI): 1.049-2.672, $P=0.031$), living in Sacheon City (OR=7.984, 95% CI: 1.566-40.706, $P=0.012$), and blood eosinophil count (OR=

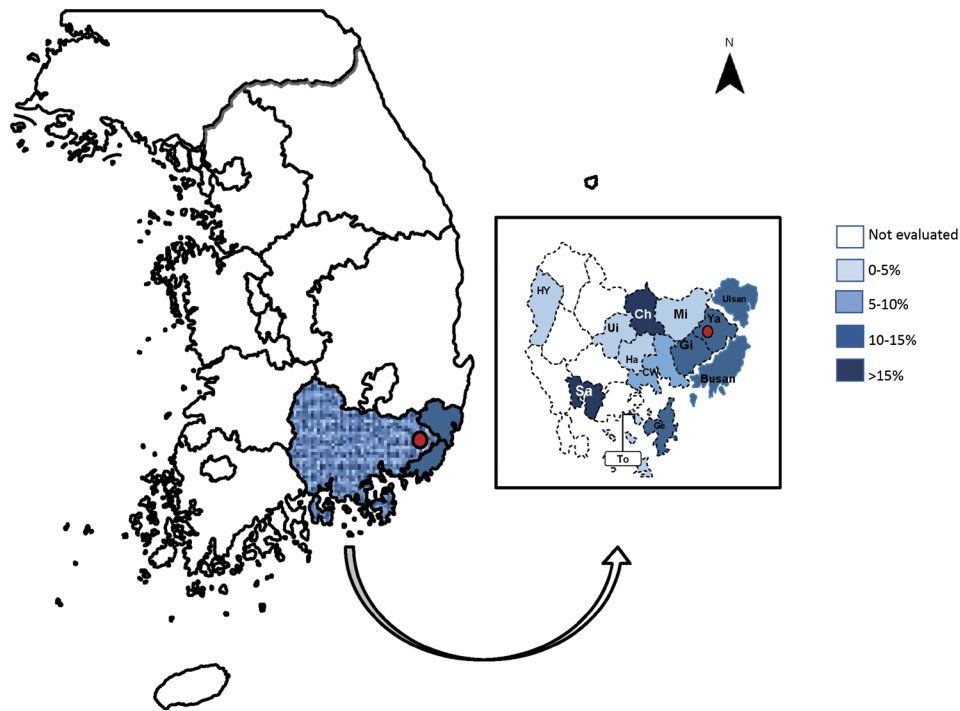


Fig. 1. Distribution of the seropositivity rate of *Strongyloides stercoralis* antibody in the southeastern region of Korea. Sa, Sacheon; Ch, Changnyeong; Ge, Geoje; Gi, Gimhae; Ya, Yangsan; CW, Changwon; Mi, Miryang; To, Tongyeong; HY, Hamyang.

Table 1. Results of *Strongyloides stercoralis* antibody testing according to age, sex, and eosinophil count

	Positive	Negative	Total (%)	<i>P</i> -value
No. (%)	92 (11.0)	742 (89.0)	834 (100)	
Age (yr, mean \pm 2 SD)	52.6 \pm 10.2	51.0 \pm 10.8	51.2 (100)	0.200
18-30	1 (5.9)	16 (94.1)	17 (2.0)	
31-40	14 (10.9)	115 (89.1)	129 (15.5)	
41-50	19 (8.1)	217 (91.9)	236 (28.3)	
51-60	33 (11.3)	259 (88.7)	292 (35.0)	
61-70	22 (18.0)	100 (82.0)	122 (14.6)	
>71	3 (7.9)	35 (92.1)	38 (4.5)	
Age >50 (yr)	62 (67.4)	415 (55.9)	477 (57.2)	0.036
Sex, Man (%)	51 (55.4)	311 (41.9)	362 (43.4)	0.014
Eosinophil (mean \pm 2 SD per mm ³)	202.1 \pm 178.9	154.8 \pm 152.0	160.0 \pm 155.8	0.006
Eosinophilia (>500 per mm ³)	9 (9.8)	26 (3.5)	35 (4.2)	0.010

1.002, 95% CI: 1.001-1.003, $P=0.003$) were found to be significantly associated with antibody test positivity. The difference in sex among the seropositive and seronegative participants was not found to be significant using the multivariate analysis (OR= 1.469, 95% CI: 0.933-2.314, $P=0.096$). However, it is speculated that men are more exposed to *S. stercoralis* infection than women, because they tend to spend more time outdoors than women [20]. Therefore, it is necessary to confirm whether the high antibody positive rate in male participants is an independent factor through a large-scale study in the future.

DISCUSSION

In Korea, there is a lack of studies on *S. stercoralis* seropositivity. However, in recent studies, seropositivity rates of the antibody were reported to be 5-46.3% in China, Japan, and southeast Asia [2,16,20-22]. The seropositive rate of *S. stercoralis* antibody in this study was 11.0%, similar to the previous study [16].

The present study was able to confirm the following: blood eosinophil count, age > 50 years, and living in Sacheon (a city located in the Gyeongangnam-do) were significantly associat-

Table 2. Seropositive rate by administrative region in the southeastern area of Korea

Administrative division	Size of the area	Population density (people/km ²)	Area (km ²)	Proportion of farm population (%)	Positive No./ Total (%)	P-value
Busan	Metropolitan city	4,349.3	770	0.8	33/323 (10.2)	0.573
Ulsan	Metropolitan city	1,074.10	1,057	3.2	17/169 (10.1)	0.783
Gyeongsangnam-do	Province	316.1	10,541	27.5	40/324 (12.3)	0.564
Sacheon	City	321.7	398.7	9.5	3/6 (50)	0.020
Changnyeong	Rural area	115.2	532.7	21.4	1/2 (50)	0.209
Geoje	City	594.4	403.8	5.1	1/7 (14.3)	0.560
Gimhae	City	1,170.70	463.4	3.8	10/71 (14.1)	0.426
Yangsan	City	705.0	485.6	2.4	18/162 (11.1)	1.000
Changwon	City	1,377.3	748.0	6.2	4/57 (7.0)	0.387
Miryang	City	129.8	798.6	18.5	0/15	0.394
Tongyeong	City	520.8	239.8	5.6	0/2	1.000
Hamyang	Rural area	53.9	725.5	29.1	0/2	1.000
Other areas					2/15 (13.3)	0.677

Table 3. Results of logistic regression analysis

	Odd ratio	95% Confidence interval	P-value
Age above 50 years old	1.674	1.049-2.672	0.031
Residents of Sacheon	7.984	1.566-40.706	0.012
Eosinophil count	1.002	1.001-1.003	0.003
Sex (Man)	1.469	0.933-2.314	0.096

ed with antibody positivity. Blood eosinophil count was significantly higher in the antibody-positive group, but only 9.8% of patients in the positive group had overt eosinophilia > 500 per mm³. This finding is similar to the results of previous studies [5,23] and showed that blood eosinophil count should not be used as a screening test. To the best of our knowledge, this study is the first report showing serum levels of *S. stercoralis* antibodies in Korea.

Notably, the positivity rate was high among the residents of Sacheon, an area where agriculture and fisheries are predominant [19]. This city is bordered by mountains to the north and sea to the south. In addition, several small streams flow through this region. At present, it is hard to properly interpret this unexpected result. Whether geographic characteristics are related to the probability of human exposure to *S. stercoralis* requires further research, including studies in populations in adjacent areas which were not included in this study.

This study included several limitations. First, the number of participants in rural areas was insufficient for analysis. Second, we could not confirm the occupations of the participants and their overseas travel history to endemic areas. Third, residents in inland areas of Korea were not included in the study. There-

fore, our data may not truly represent the seropositivity rate in Korea. Fourth, because *S. stercoralis* antibody test kit crossly reacted with *Toxocara canis* antibody [17], there is a possibility of some false positive cases.

Despite these limitations, our study has several implications. The antibody positivity rate is 11.0%, which suggests that there is a need for the antibody test for *S. stercoralis* when treating immunosuppressed patients in Korea. It would be necessary to detect specific antibody levels against *S. stercoralis* in actual clinical settings. Second, because Korea has regions with subtropical and continental climate, it is necessary to investigate the serological responses according to the climate. Last, the antibody positivity rate was not low, even among residents living in metropolitan cities. Investigations with a suitable study design that includes additional information, such as overseas travel history and exposure history, are required in the future.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

- Viney ME, Lok JB. *Strongyloides* spp. In Hodgkin J, Anderson Peds, WormBook eds, The *C. elegans* Research Community, WormBook. 2007, pp 1-15. <https://doi.org/10.1895/wormbook.1.141.1>
- Winnicki W, Eder M, Mazal P, Mayer FJ, Sengölge G, Wagner L. Prevalence of *Strongyloides stercoralis* infection and hyperinfection syndrome among renal allograft recipients in Central Europe. *Sci Rep* 2018; 8: 15406. <https://doi.org/10.1038/s41598-018-33775-3>
- Park K, Kim MS, Chang J, Kim EJ, Yoo C, Kim MJ, Sung H, Kim MN. A case of chronic strongyloidiasis with recurrent hyperinfection. *Lab Med Online* 2019; 9: 171-176 (in Korean). <https://doi.org/10.3343/lmo.2019.9.3.171>
- Keiser PB, Nutman TB. *Strongyloides stercoralis* in the immunocompromised population. *Clin Microbiol Rev* 2004; 17: 208-217. <https://doi.org/10.1128/CMR.17.1.208-217.2004>
- Kim J, Joo HS, Kim DH, Lim H, Kang YH, Kim MS. A case of gastric strongyloidiasis in a Korean patient. *Korean J Parasitol* 2003; 41: 63-67. <https://doi.org/10.3347/kjp.2003.41.1.63>
- Kim J, Joo HS, Ko HM, Na MS, Hwang SH, Im JC. A case of fatal hyperinfective strongyloidiasis with discovery of autoinfective filariform larvae in sputum. *Korean J Parasitol* 2005; 43: 51-55. <https://doi.org/10.3347/kjp.2005.43.2.51>
- Cho JY, Kwon JG, Ha KH, Oh JY, Jin MI, Heo SW, Lee GH, Cho CH. A case of steroid-induced hyperinfective strongyloidiasis with bacterial meningitis. *Korean J Gastroenterol* 2012; 60: 330-334 (in Korean). <https://doi.org/10.4166/kjg.2012.60.5.330>
- Rah YM, Yun SA, Yoon HJ, Lee SY. *Strongyloides* hyperinfection in an elderly patient treated for stomach cancer. *Ann Geriatr Med Res* 2014; 18: 241-245 (in Korean). <https://doi.org/10.4235/jkgs.2014.18.4.241>
- Seo AN, Goo YK, Chung DI, Hong Y, Kwon O, Bae HI. Comorbid gastric adenocarcinoma and gastric and duodenal *Strongyloides stercoralis* infection: a case report. *Korean J Parasitol* 2015; 53: 95-99. <https://doi.org/10.3347/kjp.2015.53.1.95>
- Won EJ, Jeon J, Koh YI, Ryang DW. Strongyloidiasis in a diabetic patient accompanied by gastrointestinal stromal tumor: cause of eosinophilia unresponsive to steroid therapy. *Korean J Parasitol* 2015; 53: 223-226. <https://doi.org/10.3347/kjp.2015.53.2.223>
- Kim JH, Kim DS, Yoon YK, Sohn JW, Kim MJ. Donor-derived strongyloidiasis infection in solid organ transplant recipients: a review and pooled analysis. *Transplant Proc* 2016; 48: 2442-2449. <https://doi.org/10.1016/j.transproceed.2015.11.045>
- Kim EJ. Acute respiratory distress syndrome with alveolar hemorrhage due to strongyloidiasis hyperinfection in an older patient. *Ann Geriatr Med Res* 2018; 22: 200-203. <https://doi.org/10.4235/agmr.18.0041>
- Ra H, Chung JW, Chung DH, Kim JH, Kim YJ, Kim KO, Kwon KA, Park DK. Strongyloidiasis presenting as yellowish nodules in colonoscopy of an immunocompetent patient. *Clin Endosc* 2019; 52: 80-82. <https://doi.org/10.5946/ce.2018.078>
- Bae J, Jeong MJ, Shin DH, Kim HW, Ahn SH, Choi JH, Yu HS. Phylogenetic positioning of a *Strongyloides stercoralis* isolate recovered from a Korean patient and comparison with other Asian isolates. *Korean J Parasitol* 2020; 58: 689-694. <https://doi.org/10.3347/kjp.2020.58.6.689>
- Youn H. Review of zoonotic parasites in medical and veterinary fields in the Republic of Korea. *Korean J Parasitol* 2009; 47 (suppl): 133-141. <https://doi.org/10.3347/kjp.2009.47.S.S133>
- Buonfrate D, Bisanzio D, Giorli G, Odermatt P, Fürst T, Greenaway C, French M, Reithinger R, Gobbi F, Montresor A, Bisoffi Z. The global prevalence of *Strongyloides stercoralis* infection. *Pathogens* 2020; 9: 468. <https://doi.org/10.3390/pathogens9060468>
- Bisoffi Z, Buonfrate D, Sequi M, Mejia R, Cimino RO, Krolewiecki AJ, Albonico M, Gobbo M, Bonafini S, Angheben A, Requena-Mendez A. Diagnostic accuracy of five serologic tests for *Strongyloides stercoralis* infection. *PLoS Negl Trop Dis* 2014; 8: e2640. <https://doi.org/10.1371/journal.pntd.0002640>
- Beck HE, Zimmermann NE, McVicar TR, Vergopolan N, Berg A, Wood EF. Present and future Köppen-Geiger climate classification maps at 1-km resolution. *Sci Data* 2018; 5: 180214. <https://doi.org/10.1038/sdata.2018.214>
- Statistical Geographic Information System. Population and household theme map list [Internet]. Available from: https://sgis.kostat.go.kr/view/thematicMap/thematicMapMain?stat_thema_map_id=sl8uqsnppF20160121115806975w5w92MFI5L&theme=CTGR_001&mapType=05&CTGRS=CTGR_001:recommend,CTGR_002:recommend,CTGR_003:recommend,CTGR_004:recommend,CTGR_005:recommend,CTGR_006:recommend (in Korean).
- Suntaravitun P, Dokmaikaw A. Prevalence of intestinal parasites and associated risk factors for infection among rural communities of Chachoengsao Province, Thailand. *Korean J Parasitol* 2018; 56: 33-39. <https://doi.org/10.3347/kjp.2018.56.1.33>
- Kobayashi J, Sato Y, Toma H, Shimabukuro I, Tasaki T, Takara M, Shiroma Y. Epidemiological features of strongyloides infection in Okinawa, Japan: comparative study with other endemic areas. *Jpn J Trop Med Hyg* 2000; 28: 9-14. <https://doi.org/10.2149/tmh.1973.28.9>
- Zhou X, James AA, Wang C, Li J, Chen X, Yan G, Xu J. Strongyloidiasis: an emerging infectious disease in China. *Am J Trop Med Hyg* 2013; 88: 420-425. <https://doi.org/10.4269/ajtmh.12-0596>
- Mirzaei L, Ashrafi K, Roushan ZA, Mahmoudi MR, Masooleh IS, Rahmati B, Saadat F, Mirjalali H, Sharifdini M. *Strongyloides stercoralis* and other intestinal parasites in patients receiving immunosuppressive drugs in northern Iran: a closer look at risk factors. *Epidemiol Health* 2021; 43: e2021009. <https://doi.org/10.4178/epih.e2021009>
- Statistical Geographic Information System. Number of agricultural workers 2020 [Internet]. Available from: https://sgis.kostat.go.kr/view/thematicMap/thematicMapMain?stat_thema_map_id=JouDrDrEIF201601211158069886Mv8uqz22x&theme=CTGR_004&mapType=05&CTGRS=CTGR_001:recommend,CTGR_002:recommend,CTGR_003:recommend,CTGR_004:recommend,CTGR_005:recommend,CTGR_006:recommend (in Korean).