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Seroprevalence and risk factors of Lyme disease among Korean deer farmers

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대한민국 사슴농가 종사자의 라임병 혈청유병률 및 위험요인

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= Abstract =

목적 : 이번 연구는 인수공통감염병의 고위험군인 사슴농가 종사자를 대상으로 라임병의 감염 실태 파악 및 위험요인 분석을 위해 수행하였다.

대상 및 방법 : 전국 시 · 군 지역의 사슴농가를 중심으로 516명에 대해 설문조사 및 혈청검사를 실시하였다. 라임병 진단방법은 IFA(Indirect Immunofluorescence antibody Assay, 간접면역형광항체법)와 IFA검사의 높은 위양성률을 보완하기 위해 ELISA 검사 그리고 Western Blot 법을 이용하였다.

결과 : 전국 사슴농가 종사자 516명의 라임병 최종 혈청 유병률은 2.3%이었으며, 엘크 (Cervus Canadensis)만을 기르는 사슴 농가 종사자의 라임병 혈청유병률이 3.6%로 다른 종류의 사슴을 키우는 사슴 농가 종사자보다 라임병 발병 위험이 통계적으로 유의하게 높았다(p = 0.033).

결론 : 국내 사슴농가 종사자들이 인수공통감염병인 라임병에 노출되어 있음을 확인하였고, 키우는 사슴의 종류나 작업 행태, 보호복 착용 여부 등에 따라 라임병 노출의 가능성이 다름을 확인할 수 있었다.

중심단어 : 라임병, 사슴농가, 혈청유병률, 인수공통감염병, 위험요인

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Introduction

Lyme disease (LD) is one of the most prevalent zoonoses worldwide and is caused by several genospecies of the spirochete *Borrelia burgdorferi sensu lato* complex. Of these genospecies, five human-pathogenic genospecies have been identified, namely, *B. burgdorferi sensu stricto, B. afzelii, B. garinii, B. bavariensis, and B. spielmanii*(1, 2). Human LD infections exhibit a wide variety of clinical manifestations from early phase erythema migrans, multiple erythema migrans, early neuroborreliosis, acute arthritis and carditis to neuro-borreliosis (meningo-radiculitis, meningitis or meningo-encephalitis), Lyme arthritis, and/or borrelia lymphocytoma, which develops several weeks after infection (3-6).

The incidence of LD is increasing in many countries, and LD is often considered an occupational disease (2, 4, 7). Previous studies have indicated those in close contact with domestic or wild animals are at elevated risk of LD (8-11), and farmers, veterinarians, forest workers, and soldiers are frequently reported to be infected (11-14). In South Korea, the first case of LD was reported in Gangwon province in 2010, and subsequently LD was designated a notifiable infectious disease (15). Over the following years the estimated annual incidence of LD in Korea has increased, for example, 3, 11, 13, and 9 cases were reported in 2012, 2013, 2014, and 2015, respectively (16). The latest study on the topic found LD is prevalent throughout South Korea and that annual case number increased from 2 in 2012 to 54 in 2017 (17).

Geographic distribution of tick vectors, climatic and ecologic factors, and individual behavior increase the risk of a tick bite and the risk of human infection (4, 18). LD is difficult to diagnose because it has a wide spectrum of clinical manifestations, and although few succumb to the disease, it can be fatal. Furthermore, no vaccine is available to prevent human infection (3, 4, 6). Thus, reducing the risk of LD probably offers a better strategy to reduce growing health concerns. However, risk reduction strategies must be derived using evidence-based information about the disease and its associated risk factors. Given the above background, we undertook this cross-sectional study to determine the seroprevalence and the risk factors of contracting Lyme disease in a cohort of Korean deer farmers.

Materials and methods

1. Study design and participants

This cross-sectional study was carried out on Korean deer farmers from 1st July to 30th September 2009. According to the Korean Ministry of Agriculture, Food, and Rural Affairs (19), 715 deer farmers comprised the Korean Deer Breeder Association, and we attempted to recruit all for the present study. However, 125 were not available during the time of data collection and 74 refused to participate. The remaining 516 consented to participate (response rate 87%) and constituted the study cohort.

2. Data collection

2.1 In-person interview

A face-to-face interview was conducted with each participant in a livestock veterinary service laboratory or the Public Health and Environment Research Institute using a structured questionnaire. The research team consisted of 3–4 members, that is, a medical doctor, a nurse, and one or two interviewers. The interviewers obtained participant baseline information, details of the nature of the work performed, and whether they used protective measures aimed at preventing LD.

2.2 Blood sample collection and examination

After completing the questionnaire, a blood sample (10 ml) was collected from each participant. These samples were centrifuged and the serum so obtained was transported to the zoonotic diseases department of the Korean Center for Disease Control & Prevention (KCDC) for analysis. Initially, samples were screened for LD seropositivity using an immunofluorescence assay (IFA) or an enzyme-linked immunosorbent assay (ELISA). Diagnoses were using a Western blot test (20). Serum titers for IgG or IgM of >1:16 by IFA or of ≥1: 24 by ELISA were considered positive for LD. Serum samples of those with a positive result by IFA or ELISA were subjected to Western blotting, and Western blot test results of ≥ 7 bands were considered seroprevalence as the outcome variable of the study.

3. Ethical considerations

This study was reviewed and approved by the Institutional Review Board of Dongguk University, Gyeongju Hospital (approval number: 09-14). All participants provided informed consent before the study was initiated. Participant privacy and anonymity were fully maintained, and all personal identifiers were removed from collated data before analysis.

4. Statistical analysis

Questionnaire responses were coded and entered into Excel. Statistical analysis was performed using SPSS ver. 18.0 (SPSS Inc. Chicago, IL, USA). Fisher's exact test, the chi-squared test, and the chi-squared test for trend analysis were used to identify associations between independent variables and seropositivity for LD (the outcome variable). Statistical significance was accepted for p-value < 0.05.

Results

Table 1. detailed the personal profile of the deer raisers associated with Lyme disease infection.

Of the 516 study subjects, only 12 (2.3%) were seropositive for Lyme disease. Although not statistically significant men had higher seropositivity rate than women (2.7%; n=410 vs. 0.9%; n=106), and those aged < 40 years (5.6%; n=18) and 50-59 years (3.3%; n=180) had higher infection rates than other age groups. Similarly, a working duration of < 19 years was associated with a higher infection rate. A significant difference was observed between LD infection rates by type of deer raised and the rate was highest for those raising Elk (*Cervus Canadensis*)

Table 1. Personal Profile of the deer raisers associated with Lyme disease infection, South Korea, 2009

Variables	Lyme Disease(-), n (%)	Lyme Disease(+), n (%)	Total, N(100%)	P-value
Gender				0.475*
Male	399 (97.3)	11 (2.7)	410	
Female	105 (98.1)	1 (0.9)	106	
Age				0.956†
<40	17 (94.4)	1 (5.6)	18	
40-49	60 (98.4)	1 (1.6)	61	
50-59	184 (98.4)	3 (1.6)	187	
60-69	174 (96.7)	6 (3.3)	180	
≧70	69 (98.6)	1 (1.4)	70	
Working duration (in years) ‡				0.081†
<10	104 (96.3)	4 (3.7)	108	

Variables	Lyme Disease(-), n (%)	Lyme Disease(+), n (%)	Total, N(100%)	P-value
10-19	234 (97.1)	7 (2.9)	241	
20-29	117 (99.2)	1 (0.8)	118	
≧30	39 (100)	0 (0.0)	39	
Types of deer raised ‡				0.033
Beautiful spotted deer *(Axis axis)*	140 (100.0)	0 (0.0)	140	
Beautiful spotted deer *(Axis axis)* + Elk *(Cervus Canadensis)*	134 (97.1)	4 (2.9)	138	
Elk *(Cervus Canadensis)*	211 (96.3)	8 (3.7)	219	

※ Fisher's exact test; † chi-squared test for trend analysis; ‡ excluding those that could not recall working duration and could not answer the types of deer raised

(3.7%; n=138) followed by those raising Beautiful spotted deer (Axis Axis) and ElK (Cervus Canadensis) (2.9%; n=138) (p=0.033).

A summary of associations between work-related factors and LD infection is provided in Table 2. Deer farmers involved in management of livestock sheds (2.5%; n=486), feeding deer (2.4%; n=490), removing excrement (2.5%; n=398), processing industry (2.7%; n=148), and in the processing of compost (2.5%; n=355) had higher LD infection rates but without significance.

Associations between LD and the use of personal protective measures and work-hygiene related factors as summarized in Table 3. Those who did not use protective glasses and a mask were found to be at higher risk of LD infection (2.4%; n=502). Similarly, those who did not use protective gloves and an apron (2.7%; n=186) or boots (2.6%; n= 196) had higher

Table 2. Work-related factors of the deer raisers associated with Lyme Disease infection, South Korea, 2009

Variables	Lyme Disease (-), n (%)	Lyme Disease (+), n (%)	Total, N (100%)	P-value
Management of the livestock shed				1.000*
Yes	474 (97.5)	12 (2.5)	486	
No	30 (100.0)	0 (0.0)	30	
Feeding deer				1.000*
Yes	478 (97.6)	12 (2.4)	490	
No	26 (100.0)	0 (0.0)	26	
Removing excrement				1.000*
Yes	388 (97.5)	10 (2.5)	398	
No	116 (98.3)	2 (1.7)	118	
Processing industry (deer extract)				0.750*
Yes	144 (98.3)	4 (2.7)	148	
No	360 (97.8)	8 (2.2)	368	
Processing of compost				0.762*
Yes	346 (97.5)	9 (2.5)	355	
No	158 (98.1)	3(1.9)	161	

※ Fisher's exact test

rates of infection. Regarding work-hygiene related factors, those that did not disinfect work instruments (3.3%, n=153) and those that did not shower after work (3.1%; n=160) had higher infection rates.

Table 3. Personal protective measures and work-hygiene factors of deer farmers and the risks of Lyme disease infection, South Korea, 2009

Variables	Lyme Disease (-), n (%)	Lyme Disease (+), n (%)	Total, N (100%)	P-value*
Use of protective measures				1.000
Protective glasses and masks				
Yes	14 (100.0)	0 (0.0)	14	
No	490 (97.6)	12 (2.4)	502	
Protective gloves and aprons				0.764
Yes	323 (97.9)	7 (2.1)	330	
No	181 (97.3)	5 (2.7)	186	
Boots				0.772
Yes	313 (97.8)	7 (2.2)	320	
No	191 (97.4)	5 (2.6)	196	
Work-hygiene- related				
Disinfection of used instruments				0.352
Yes	356 (98.1)	7 (1.9)	363	
No	148 (96.7)	5 (3.3)	153	
Shower after work				0.528
Yes	349 (98.0)	7 (2.0)	356	
No	155 (96.9)	5 (3.1)	160	

※ Fisher's exact test

Discussion

The present study reports for the first time the seroprevalence and the factors that increase the risk of contracting Lyme disease among South Korean deer farmers. Twelve (2.3%) of the 516 deer farmers enrolled were seropositive for Lyme disease. The seroprevalence of LD among the different risk groups depends on exposure status, risk behavior, and other ecological factors as well as the study methodology adopted (4, 14). For example, it was reported in a study conducted in Serbia that seroprevalence of LD in forestry workers and soldiers were 11.76% and 14.14%, respectively (14), and in a Polish study conducted among forestry workers and soldiers while seroprevalence ranged between 18.2% and 50.7% (11). Thus, the present study indicates Korean deer farmers have a markedly lower seroprevalence rate. Nonetheless, as the incidence of LD in South Korea exhibits a positive trend (17), high risk groups require careful surveillance and evidence-based preventive strategies are needed to reduce the growing burden imposed by LD.

Importantly, we found Elk (*Cervus Canadensis*) deer farmers were at significantly greater risk of having LD than farmers of other types of deer. In South Korea, domestic animals, including horses and dogs, have been reported to be infected with *Borrelia burgdorferi*, which suggests periodic health checkups be performed on individuals that work closely with animals (21-23). Furthermore, it has been confirmed that Borrelia-infected ticks infest wild Korean water deer (*Hydropotes inermis Swinhoe*) (24), which suggests the possibility that ticks harboring Borrelia burgdorferi might have transmitted infection to

ElK(*Cervus Canadensis*). Further animal and genetic studies are required to determine whether Korean Elk (*Cervus Canadensis*) are infested with ticks harboring *Borrelia burgdorferi.*

In addition, we also found socio-demographic factors such as a male gender, an age of < 40 years, and a work history of <19 years were non-significantly associated had higher rates of LD infection, which concurs with that found in a previous study (25). It can be expected that male gender and the shorter the working period, the less competence to wear protective gear and the less likely to be prepared for exposure to ticks. In addition, we found individuals involved in the management of livestock sheds, deer feeding, processing industry, and composting and those that did not use protective measures (e.g., glasses, masks, protective gloves, and aprons), and those that did not disinfect work instruments and shower after work had higher LD rates. Although these work and preventative measure factors were not found to be statistically significant, the increasing incidence of LD suggests these factors be taken into account by those designing preventive strategies for deer farmers.

Some limitations of the present study require consideration. First, although we analyzed relations between different farm activities and LD seropositivity, numbers of detected positive cases were too small to allow us to calculate odds ratios. Second, the self-report information used may have introduced bias. Nevertheless, the study had a high response rate and a nationally representative sample was enrolled, which enables generalization of our findings at a national level.

Summary

This study was undertaken to determine the seroprevalence and risk factors associated with contracting Lyme disease (LD) among Korean deer farmers. This cross-sectional study devised questionnaire that addressed farm activities, was devised and the blood samples of 516 Korean deer farmers were tested. LD seroprevalence was determined by Western blot test. Fisher's exact test, the chi-squared test, and the chi-squared test for trend analysis were performed to assess the risk associated with LD. Of total 516 study participants recruited, only 12 (2.3%) were seropositive for LD. The result of the study revealed that only deer farmers raising Elk (*Cervus Canadensis*) were found to be at significantly higher risk of contracting LD than other deer farmers (p=0.033). In addition, a male sex, an age of < 40 years, and those that had raised deer for < 19 years had higher rates of LD infection than their counterparts. Similarly, those that managed livestock sheds, fed deer, processed industry and prepared compost had higher rates of LD infection. In terms of protective factors, those who did not use protective measures such as wear glasses and masks, or protective gloves and aprons, and those that did not disinfect work instruments and did not shower after work had higher rates of LD than those that used protective measures. In conclusion, preventive health strategies should take into account the profiles of deer farmers at greater risk based on considerations of personal, type of work, and the use of personal protective measures.

Authors' contributions

KL, JHC and SYJ conceptualized the study. DA and SYJ analyzed the data and wrote the manuscript (with important contributions from JHP and JHC). All authors participated in the writing and the revision of the manuscript and in the analysis and interpretation of results. All authors read and approved the final version of the manuscript.

Conflict of interest

The authors have no conflict of interest to declare.

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