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TRENDS IN EPIDEMIOLOGICAL ASPECTS OF LYME DISEASE WITH DOMESTIC AND EXOTIC INFECTIONS IN REPUBLIC OF KOREA, 2011-2017

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ABSTRACT

Background and Methods: This study focuses on a quantitative analysis of the epidemiological aspects of Lyme diseases (LD) with domestic and exotic infections in Republic of Korea (ROK). A total of 96 cases including domestic and exotic infections were 54 and 42 infections from 2011 to 2017. Especially, a total of 42 cases of imported exotic LD notifications were introduced from endemic foreign countries. The raw data obtained from the Korea Center for Disease Control and Prevention (KCDC). **Results:** Nationwide, the cumulative incidence rate (CIR) of LD was 0.027 per 100,000 populations; the CIR of LD with domestic and exotic cases was 0.015 and 0.033 per 100,000 populations, respectively. When compared, the CIR of domestic cases of LD was much lower than that in exotic cases ($p<0.01$). In addition, the exotic-to-domestic morbidity ratio (EDCR) was 0.78. During the same period, a CIR of LD in metropolitan area of Seoul (0.044) was higher than that of counties (0.023) in ROK ($p<0.05$). In the total case-fatality rate of LD was 1.04 %. On the other hands, our results also show that the male-to-female morbidity ratio (MFMR) was 0.66. More women was infected with LD than men ($p<0.05$). Individuals aged 40-59 years were most infected than those of other ages (42.7%, $p<0.01$). About four-fifths of reported LD cases occurred between June and November in year. Most imported exotic LD cases were associated with in Americas region (22 cases or 52.4% of total cases). The number of reported cases with LD has been increasing since from 2011 up to now. Conclusion: To prevent LD infections, greater attention should be paid to individuals who are the planning to presumptive areas.

KEYWORDS: Domestic and Exotic LD, CIR, epidemic aspects, presumptive origins.

INTRODUCTION

Lyme disease (LD) or Lyme borreliosis is the most prevalent tick-borne zoonosis and an important emerging infection in North America, Europe, and Far Eastern Asia including Korea and Japan.[1- 4] The etiological agents by infection with at least three spirochete species include *Borrelia burgdorferi, B. garinii* and *B. afzelii*. Human Lyme borreliosis is vectored by *Ixodes* ticks, specifically *Ixodes scapularis, I. ricinus, I. pacificus* and *I. persulcatus.*[1,3, 4-6] *Ixodes persulcatus* is predominantly in Russia and Far East Asia, and has been implicated as a vector of several human pathogens including LD.[5,6] The majority of patients with LD develop a characteristic rash, erythema migrans, accompanied by symptoms of fever, malaise, fatigue, headache, myalgia, or arthralgia[1-4] LD was first described in 1975 following investigation of a cluster of arthritis cases among children living near Lyme, Connecticut in the United States.[1,3,5,7] In the ROK, the first identified case of autochthonous Lyme disease case after designation to the national notifiable disease in 2012, and classified as a Category IV Notifiable Infectious Disease by the Korea Center for Disease Control and Prevention (KCDC).[2] LD occurs naturally in reservoir host, including mice, squirrels, shrews, and other vertebrates including birds.[1,4,5,8] *Borrelia burgdorferi*, the causative agents of LD, is of considerable concern to all of us and the veterinary profession is deeply involved in and is playing a most important part for public health service studying.[1 – 5]

It is highly probable that exotic LD infections were introduced to the ROK through an increased number of travelers to the ROK through an increased number of travelers to affected countrie which is strictly controlled by the KCDC.[2,9,10] Therefore, the objective of this study was to describe the epidemiology of LD cases that were reported in the ROK from 2011 to 2017, in order to identify a target population to intervene and to address the ecological association between the number of domestic LD cases and exotic infections of overseas travelers. We extracted reported data regarding LD infections between 2011 and 2017 from the Disease Web Statistical System of KCDC.[9]

The present study is significant because it is may be the few describe to the epidemiological aspects of Lyme disease with domestic and exotic infections in the ROK.

MATERIAL AND METHODS

We analyzed reported cases of Lyme diseases (LD) with domestic and exotic infections in the ROK; a total of 96 cases including domestic and exotic infections were 54 and 42 infections from 2011 to 2017. Especially, a total of 42 cases of imported exotic LD notifications were introduced from endemic foreign countries. We utilized the raw data from the national notifiable disease surveillance system (website) of the KCDC, 2011-2017, the ministry of Health and Welfare, Republic of Korea.[9,10]

It is our intention to study; trends in epidemiological aspects of LD with domestic and exotic infectious cases in the ROK under the following nine headings: cumulative incidence rate (CIR) including domestic and exotic cases, and habitat, exotic-to-domestic morbidity ratio (EDMR), case-fatality rate (CFR), and relative risk factors including gender, male-to-female morbidity ratio (MFMR), age, and seasonality, and cases of exotic LD imported from presumptive origins.

In this study, the cumulative incidence rate (CIR) of LD cases per 100,000 populations estimated by the criteria that World Health Organization (WHO) established, and the upper and lower limits of the 95% confidence interval (95% CI) were calculated. Statistically significant differences between the epidemiological aspects and risk factors were determined using the Pearson's chi-square test or paired *t*-test. All data analyses were performed in Microsoft Excel 2010 (Microsoft Co. Redmond, WA, USA). Results were considered statistically significant for *p*-value less than <0.05.

RESULTS AND DISCUSSION

As Table 1 show, we analyzed reported cases of LD with domestic and exotic infections in the ROK; a total of 96 cases including domestic and exotic infections were 54 and 42 infections from 2011 to 2017. Especially, a total of 42 cases of imported exotic LD notifications were introduced from endemic foreign countries. Nationwide, the cumulative incidence rates (CIR) per 100,000 populations of LD infections was 0.027 LD with domestic and exotic cases was 0.015 and 0.033, respectively. When compared, the CIR of domestic cases of LD was much lower than that in exotic cases (p<0.01). This difference could be divergence due to the difference in source and mode of infections between the natural and artificial living environment, and so many cases of LD infections among travelers returning from the presumptive origins of exotic LD in overseas.[1-6, 9,10] During the same period, the exotic-to-domestic morbidity ratio (EDCR) was 0.78. This is the epidemiological meaning that the imported exotic LD had higher levels of incidence with exotic LD infections. For example, the CIR and EDCR of LD in Japan between 2006 and 2010 were 0.008 per 100,000 populations and 0.2.[4]

Moreover, the CIRs of LD cases in the metropolitan of Seoul in the ROK were 0.044 per 100,000 populations and that in counties was 0.023. When compared, the CIR of LD in metropolitan (Seoul) was significantly higher than that of counties in the ROK (p<0.05). These differences could attributed to divergence of the source and mode of infections in the natural or artificial living environment in the domestic cases of LD and so many cases of infections among travelers returning from the presumptive origins of LD overseas [1-4, 6,9,10]. Particularly, in metropolitan area, LD ranked as the most common imported infectious disease from overseas than in counties.[3,4,9]

On the other hands, the CFR of LD infections in South Korea was 1.04 %. It is lower level of the other zoonoses that in WHO reports.[1,3] These data strongly indicate that the most cases of LD can be treated successfully with a few weeks of antibiotics.[1,3,4,9,11]

Table 2 shows the epidemiological relative risk factors of LD cases that occurred in the ROK between 2011 and 2017; analyzed by gender, male-to-female morbidity ratio (MFMR), age, and seasonality outbreaks of LD. Our results also shows in analyzed LD cases that significantly more women were infected compared to men (men: 39.6% vs. women: 60.4%, MFMR: 0.66), (p<0.05). These remarkable differences in gender distribution are believed to reflect cultural differences in terms of lifestyle in the field activities in farming, clothes and ornamentation in Korean customs and the number of overseas travels. However, for example, in the case of the United States, during the period from 1992 to 2006, information about sex was available for 243,564 reported cases. Of these, 129,349 (53.1%) occurred among males yielding an average annual rate per 100,000 population of 6.3 cases for males and 5.4 cases for females.[1] In additionally, in the case of Japan among the 49 cases (male: 31 cases or 63.3% vs. female: 18 cases or 36.7%) of LD including domestic and exotic infections were 41 and 8 infections from 2006 to 2010. Trends in the incidence rates of LD increased disproportionately among males compared with females in the Japan and the USA.[1,4]

The distribution of LD cases by age-specific adjusted groups was as follows: for the age groups of under 19, 20-39, 40-59, and over 60 years old the percentages were 8.3%, 33.3%, 42.7% and 15.8%, respectively (p<0.01) and a the highest infections of LD was observed in those aged more than among the 20-59 years old group (76.0%), which clearly shows a significantly higher incidence of LD in the prime of lives (p<0.01). However, we have an additional information regarding reports from Japan. Since April 2006 when the notification criteria were amended, 49 cases were reported till December

2010. Among the 49 cases, 41 cases were domestic cases and 21 (51.2%) of them were those older than 60 years.[4] In additions, the information from the USA, age-specific groups ranged from 1 to 101 years and were bimodal in distribution that the average annual rates peaked among children aged 5-9 years (8.6 per 100,000) and adults aged 55-59 years (7.8 per 100,000). The lowest rate was reported among adults aged 20-24 years (3.0 per 100,000) [1]. These differences could attributed to divergence of the source and mode of infections with the living environment among the domestic cases of LD from the presumptive origins.[1-4,9,10]

We analyzed the seasonal pattern of reported LD cases in Korea, found that 10.4% of the cases occurred in spring, 37.5% in summer, 39.6% in autumn, and 12.5% in winter, demonstrating significant seasonal variation in the distribution of the cases ($p<0.01$). During the period, reported cases increased markedly in June, peaked in July through November, and began decreasing in the early of December to March of the next year with the cold season. In the U.S., in all months of the year; the majority (25.8% of 48,413 cases) of patients had an onset in June, July (30.0%), or August (12.1%), the 3 months in which ticks actively seek mammalian hosts and human outdoor activity is greatest.[1,12] In the case of Japan, the number of reported cases is highest in July and almost absent in winter season from December to March of the next year.[4]

On the other hand of remarkably, LD is causes by infection to genus *Borrelia*. It is transmitted to humans by tick bite during outdoor activities. For example, LD in the USA is caused mainly by *Borrelia burgdorferi*, while in Europe it is caused by *B. burgdorferi*, *B. garinii*, *B. afzelii*, and Japan by *B. garinii*.[1-4] Table 3 shows, the presumptive origins for the exotic LD infections in the ROK were Americas region included 3 countries (22 cases or 52.4% of the total cases), Europe region included 9 countries (12 cases or 28.6%), Asia region included 5 countries (5 cases or 11.9%), Middle East region 2 countries (2 cases or 4.8%) and unknown (1 cases or 2.4%), respectively. Specifically, more than half of the LD cases were infected from the U.S.A. (18 cases or, 42.9% of total cases), Canada (3 cases or 7.1%), Germany, Sweden and Italia (each 2 cases or each 4.8%), respectively. Remarkable, it is may be the number of reported exotic LD cases over the study period was highly relationship with the number of overseas travelers. The most frequently suspected origin as the origin of infections was Americas and Europe regions ($p<0.01$). It is may be these data strongly indicated that Koreans tend to travel developed countries where the risk for LD is significantly higher than in other countries. Therefore, the incidence of imported exotic LD is influenced by travel destinations. In additions, the information from Japan, there was an 8 cases infected abroad, such as the United States (4 cases), Germany (3 cases) and Switzerland (1 case), respectively.[4] This is a similar distribution of the patterns among LD with imported exotic infections between the ROK and Japan.[4,9,10]

Finally, the number of reported cases of LD continues to increase in the ROK, underscoring the need for targeted prevention strategies, early disease recognition and treatment, and a sustainable surveillance system. During the seven-year study period, incidence increased disproportionately among elderly persons. Moreover, despite the limitations of national surveillance data, these finding of epidemic aspects are useful in defining demographics, distribution, and trends in LD cases.

In conclusion, we observed that there is a similar pattern of epidemiological aspects of LD cases in the ROK. These results underscore the continued emergency of LD and provide a basis for targeting prevention campaigns to population with increasing incidence. For example to prevent possible LD transmission from ticks, use insect repellents. Proper wear of clothing will also prevent transmission if you tuck your pants into your booth, shirt into your pants, and keep sleeves rolled down.[1-5, 11-13] Added more, for the time being travelers should pay special attention concerning LD in the North America and Europe where infections of travelers have been reported.[1-4,9-13] Moreover, we hope that this information will be a useful reference in the further study of LD.

Table 1: Trends in epidemiological aspects of Lyme disease with domestic and exotic cases in the ROK from 2011 to 2017.

Item	No. of cases (%)	CIR[1)] (96% CI)[#]
Infectious cases		
Total Cases[1)]	96	0.027 (0.022-0.032)
Domestic cases[1)]	54 (56.2)	0.015 (0.011-0.019)
Exotic cases[2)]	42 (43.8)	0.033 (0.023-0.043)
p-value		<0.01
EDMR[3)](E/D)	0.78	
Habitat		
Metropolitan area	31 (32.3)	0.044 (0.029-0.059)
Counties	65 (67.7)	0.023 (0.018-0.028)
P-value		<0.05
Case-fatal		
No. of death	1	-
CFR[4)]	1.04	

[1] CIR: Cumulative incidence per 100,000 populations.
[2] Exotic cases per 100,000 travelers.
[3] EDCR: Exotic-to-domestic morbidity ratio.
[4] CFR: Case-fatality rate in %.
[5] Chi-squared analysis indicated a significant from the total value, $p<0.05$ and 0.01.
[#] 95% CI: 95% confidence interval of the rate.

Table 2. Trends in the epidemic risk factors of Lyme disease infectious cases in the ROK from, 2011 to 2017.

Item	Cases (%)	95%, CIs
Total infectious cases	95	
Gender		
Male	38 (39.6)	29.8-49.4
Female	58 (60.4)	50.6-70.2
p-value	<0.05	
MFMR[1](M/F)	0.66	
Age-specific adjusted		
<19	8 (8.3)	3.1-14.5
20-39	32 (33.3)	23.9-42.7
40-59	41 (42.7)	32.8-52.6
>60	15 (15.6)	8.3-22.9
p-value	<0.01	
Seasonality		
Spring	10 (10.4)	4.3-16.7
Summer	36 (37.5)	27.8-47.2
Autumn	38 (39.6)	29.8-49.4
Winter	12 (12.5)	5.9-19.1
p-value	<0.01	

[1]MFMR: Male-to-female morbidity ratio. The other footnotes are Table 1.

Table 3: Presumptive origin of imported exotic Lyme disease cases in overseas travels in the ROK from 2011 to 2017.

Presumptive regions	Cases (%)	No. of countries
Asia	5 (11.9)	5
Americas	22 (52.4)	3
Europe	12 (28.6)	9
Middle East	2 (4.8)	2
Unknown	1 (2.4)	1
Total	42	20

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