



Epidemiology and Risk Factors of Lyme Disease in Taiwan from 2007 to 2020

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Background: Lyme disease or Lyme borreliosis is the most commonly transmitted tick-borne infection in the United States and among the most frequently diagnosed tick-borne infections worldwide. Lyme disease is caused by *Borrelia burgdorferi*. **Aim:** In this study, we explored the epidemiological characteristics, differences, and trends in domestic and imported cases of Lyme disease in Taiwan between 2007 and 2020 according to patient sex, age, month of confirmation, and area of residence. **Methods:** We analyzed publicly available annual summary data on domestic cases of Lyme disease from 2007 to 2020 obtained from a Taiwanese Centers for Disease Control (TCDC) database. In total, 17 confirmed imported cases of Lyme disease were reported. **Results:** Cases in individuals aged 20–59 years gradually increased, and a distinct pattern of seasonal variation (summer) was observed as a potential risk factor. Furthermore, more men had domestically acquired Lyme disease, and cases were identified in individuals living in the Taipei metropolitan area (11 cases [64.7%]) and rural areas (Gao-Ping region, three cases [17.6%]). Imported cases originated in North America (11 cases [64.7%]) and Europe (6 cases [35.3%]). The incidence of Lyme disease per million population was 0–0.13. The incidence of Lyme disease increased from 2007–2013 to 2014–2020, indicating that the recentness of imported cases may be a risk factor. **Conclusion:** This is the first study to compare imported cases of Lyme disease from 2007 to 2020 from the surveillance data of the TCDC database. This study highlights the essentiality of longitudinal and geographically extended studies in understanding zoonotic disease transmission in Taiwan. Our findings may inform future surveillance and research efforts.

Key words: Lyme disease, *Borrelia burgdorferi*, hard tick

INTRODUCTION

Lyme disease is the most clinically predominant infectious zoonosis transmitted through ticks.¹ The disease pathogen *Borrelia burgdorferi* mainly lives in wild rodents and mammals, which serve as reservoir hosts. The earliest documented case of this disease was in Europe.² However, it was not given the name Lyme disease until an epidemic of the disease occurred in Old Lyme, Connecticut, in the northeastern United States.³ At that time, the Lyme disease was considered to be an epidemic of atypical arthritis.

Approximately 30,000 cases of Lyme disease are reported annually to the American Centers for Disease Control and Prevention by State Health Departments and Health

Departments in the District of Columbia. However, estimates obtained through other methods suggest that approximately 476,000 people actually contract Lyme disease annually in the United States.⁴ The epidemic spreads across 46 American states and annually peaks from June through September. Detailed medical case reports of the disease, isolation of its pathogens, and confirmation of vector tick species have been completed in Europe,⁵ the former Soviet Union,⁶ Japan⁷ - which is geographically close to Taiwan - South Korea,⁸ and China.⁹

The *B. burgdorferi* pathogen lives mainly in the intestines of vector ticks, and humans develop Lyme disease as a

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result of opportunistic infections through the bite of infected ticks. People are more likely to contract the disease if they work outdoors in an epidemic area, participate in outdoor camping activities, or have a pet, which is a medium of transmission.¹⁰ The main vector tick species are *Ixodes dammini*, *Ixodes scapularis*, and *Ixodes pacificus* in the United States¹¹ and *Ixodes ricinus* in Europe;¹² however, similar *Ixodes* species can be found in other places. Ticks suck blood from hosts to survive and reproduce, and they transmit *B. burgdorferi* to hosts during each stage of the blood-sucking process [Figure 1]. The disease's transmission is transstadial in ticks; *B. burgdorferi* remains in an infected tick from its larval stage through the nymphal or adult stages.¹³ Generally, the blood-sucking process is completed approximately 2–3 (in the larval stage), 3–5 (in the nymphal stage), or 5–7 (in the adult stage) days after a tick attaches to the host. Adult ticks, which are relatively large (approximately 3–5 cm in length), can be easily spotted and can thus be generally removed at an early stage of attachment. Larval ticks typically attach to wild hosts and are less likely to come into contact with humans. Nymphal ticks (approximately 1–1.5 mm in length) are reported to be the primary cause of human infections because they are less visible to the naked eye and people cannot feel them attaching to their bodies.¹⁴

Lyme disease leads to various systemic lesions in the body. Most patients with Lyme disease (60%–80%) develop a skin rash at the site of the bite 3–32 days (an average of 7–10 days) after they were bitten by an infected tick.¹⁵ As *B. burgdorferi* proliferates and spreads, the skin rash gradually expands and forms erythema chronicum migrans, which has a diameter of 5 cm and a white area in the center.¹⁶ Early symptoms of the infection are similar to

those of a cold and include a headache, fever, chills, and bodily fatigue. However, if not diagnosed and treated in a timely manner, patients may develop lesions in the cardiac muscle, neurological system, and knee joints. Common clinical comorbidities include heart block, pericarditis, asymmetric arthritis of the knee, and Bell's palsy.¹⁷ The rate of comorbidity development is associated with the duration of infection.

Taiwan, located 23°4' North and 121°0' East, has a subtropical climate with a monthly average temperature of 16°C–29°C and a monthly average relative humidity of 75%–90%. As a developed country, Taiwan has a gross domestic product of US\$ 32,219.¹⁸ Although no domestic case of Lyme disease has been reported in recent years, Taiwan has had several imported cases of the disease, indicating that measures aimed at confining or eliminating the disease have had limited effectiveness. All of the imported cases in Taiwan have been sporadic, and no cluster infection has been reported. However, Taiwanese epidemic research on the risk of contracting Lyme disease by using big data is scarce. Therefore, this study employed the Taiwan National Infectious Disease Statistics System (TNIDSS)¹⁹ to evaluate the imported cases of Lyme disease from 2007 to 2020 with respect to their epidemic characteristics - the patients' sex, age, season of infection, and place of residence - and differences and any trends in the Lyme disease infections.

MATERIALS AND METHODS

Ethics

This study was approved by the Research Ethics Committee of National Taiwan University (IRB No. 202203EM033).

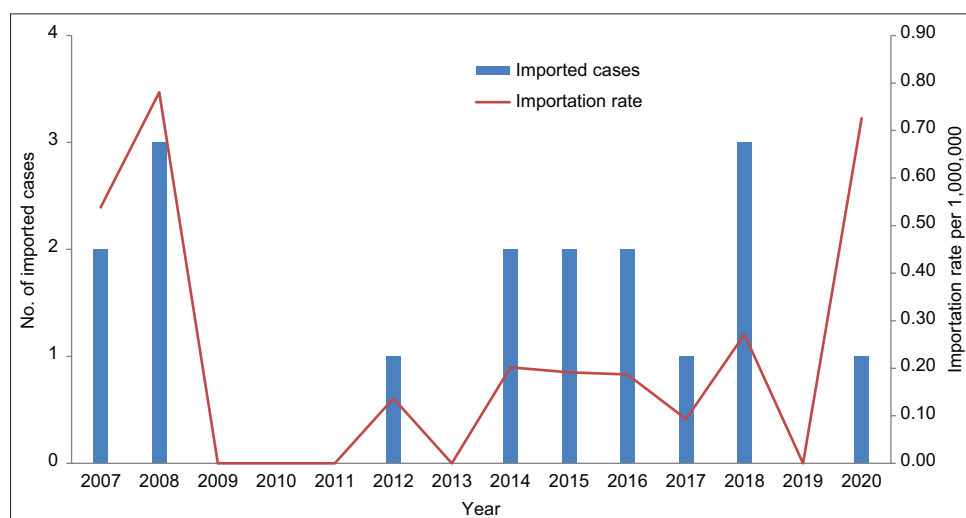


Figure 1: Number and importation rate of Lyme disease cases reported in Taiwan from 2007 to 2020

Definition of confirmed cases

In Taiwan, Lyme disease is a notifiable communicable disease, which is a disease classification outlined by the central government in the Communicable Disease Act.²⁰ The Taiwanese central government also classified Lyme disease as a Category 4 communicable disease in the Communicable Control Act in 2007. For such diseases, doctors or medical institutions must report confirmed cases to the health authorities and enact measures such as treatment or event isolation. Notifiable communicable diseases are typically characterized by rapid spread, severe symptoms, or high morbidity rates. Therefore, when doctors encounter patients suspected to have Lyme disease, they must report the patients to the health authorities within 7 days. Patients suspected to have Lyme disease exhibit clinical conditions associated with the disease (i.e., acute fever $\geq 38^{\circ}\text{C}$, headache, swollen lymph glands, muscle pain, sore throat, neck stiffness, migratory erythema, and nerve root inflammation, which appear in the later stages of the disease) as well as meet an epidemiological condition (i.e., a history of travel to places with Lyme disease). Such patients receive a test at the hospital, and the test results are deemed positive if one of the following conditions are met: (1) the separated clinical specimen (skin lesion or cerebrospinal fluid and joint capsule fluid) contains *B. burgdorferi*, which is indicated by a positive nucleic acid test; (2) acute-phase serum (or serum collected at the first time) tests positive for one of two antibodies (i.e., IgM or IgG) against *B. burgdorferi*. Positive polymerase chain reaction bacterial test results could also indicate the presence of nonlive *B. burgdorferi*. In this study, epidemiological information and clinical characteristics in addition to positive polymerase chain reaction results were considered in defining Lyme positivity in patients. According to the Taiwanese Centers for Disease Control (TCDC), for a case of Lyme disease to be confirmed, it must meet one of the aforementioned criteria.

Data source

In this study, we used the TNIDSS, a public database established by the TCDC.²¹ To ensure information security and privacy, the database includes only secondary data (i.e., notification date, onset date, confirmation date, and the number of confirmed domestic and imported cases of Lyme disease) and does not include case details. The database does not contain the patients' medical histories, their signs and symptoms, and laboratory results.

In addition, we used the Tourism Statistics Database of the Taiwanese Tourism Bureau to compile the annual number of tourists who visited Taiwan from 2007 to 2020 to calculate the annual importation rate of Lyme disease.²²

Data analysis

This was a retrospective, historical study of all cases of imported Lyme disease since 2007. We determined the number of people given a diagnosis of Lyme disease from 2007 to 2020 and analyzed the distribution of their clinical characteristics (sex, age, time of diagnosis, living area), the differences in these characteristics, and results. We then focused on sex, age, time of diagnosis, changes in living area, trends, and related results for analyses of cases of Lyme disease from 2007 to 2013 and from 2014 to 2020. The descriptive data are presented as means and summary, where appropriate. Categorical variables were compared using the Chi-square test. All statistical analyses were performed using SPSS (IBM SPSS version 21; Asia Analytics Taiwan, Taipei, Taiwan). All statistical tests were 2-sided, with a Cronbach's α value of 0.05 and significance set at a $P < 0.05$.

RESULTS

Study population

During the study period, 17 confirmed imported cases involving 11 (64.7%, 11/17) men were analyzed. Among the cases, 1 (5.9%, 1/17) was aged <19 years, 15 (88.2%, 15/17) were aged 20–59 years, and 1 (5.9%, 1/21) was aged ≥ 60 years. The cases (including three in spring, ten in summer, three in fall, and one in winter) were screened for Lyme disease. The characteristics of the confirmed cases (including area of residence) are presented in Table 1.

Epidemiological features

Lyme disease was detected more often in confirmed cases in men in 2007–2013 and in 2014–2020 (66.7%, 4/6 and 63.6%, 7/11, respectively). Lyme disease was detected more often in the 20–29 and 50–59 years age group in 2007–2013 and in the 30–39 years age group in 2014–2020. Lyme disease was detected more often in summer in 2007–2013 and in 2014–2020 (66.7%, 4/6 and 54.5%, 6/11, respectively). Lyme disease was detected more often in the Taipei area in 2007–2013 and in 2014–2020 (50%, 3/6 and 72.7%, 8/11, respectively). The data are presented in Table 2.

The annual numbers of imported cases of Lyme disease over the study period are as follows: one in 2007, three in 2008, one in 2012, two in 2014, two in 2015, two in 2016, one in 2017, three in 2018, and one in 2020 [Figure 1]. The sex, age, season of infection, and infection rate at the place of residence of these imported cases within the study period are depicted in Figure 2.

Table 3 presents the countries from which the cases were imported, which are also listed as follows: four cases from the

Table 1: Epidemiological features of imported Lyme disease cases in Taiwan from 2007 to 2020 ($n=17$)

Variables	Imported cases, n (%)
Sex	
Male	11 (64.7)
Female	6 (35.3)
Age group	
<20	1 (5.9)
20-29	4 (23.5)
30-39	4 (23.5)
40-49	2 (11.8)
50-59	5 (29.4)
≥ 60	1 (5.9)
Season	
Spring	3 (17.6)
Summer	10 (58.8)
Fall	3 (17.6)
Winter	1 (5.9)
Residency	
Taipei area	11 (64.7)
Northern	-
Central	1 (5.9)
Southern	1 (5.9)
Gao-Ping area	3 (17.6)
Eastern	1 (5.9)

United States and one from Denmark in 2007–2008, one from the United States in 2012, one from the United States and one from Germany in 2014, one from the United States and one from the United Kingdom in 2015, one from the United States and one from Sweden in 2016, one from an unknown country in 2017, two from the United States and one from Sweden in 2018, and one from the United States in 2020. In total, 11 cases were imported from North America, and six were imported from Europe. Of those, 11 were from the United States, two were from Sweden, one was from Denmark, one was from the United Kingdom, one was from Germany, and one was from an unknown country [Figure 3].

DISCUSSION

Zoonoses are diseases that can be transmitted between animals and humans. Pathogens can be transmitted directly between humans and animals or be carried by vectors to enter another organism. Zoonotic pathogens can be categorized into viruses, bacteria, molds, parasitic worms, and protozoa; they can be transmitted through contact, inhalation, or consumption

Table 2: Epidemiological features of a survey of imported Lyme disease cases in Taiwan from 2007–2020

Variables	2007–2013 year ($n=6$), n (%)	2014–2020 year ($n=11$), n (%)	P
Sex			
Male	4 (66.7)	7 (63.6)	0.901
Female	2 (33.3)	4 (36.4)	
Age group			
<20	-	1 (9.1)	0.133
20-29	3 (50)	1 (9.1)	
30-39	-	4 (36.4)	
40-49	-	2 (18.2)	
50-59	3 (50)	2 (18.2)	
≥ 60	-	1 (9.1)	
Season			
Spring	2 (33.3)	1 (9.1)	0.312
Summer	4 (66.70)	6 (54.5)	
Fall	-	3 (27.3)	
Winter	-	1 (9.1)	
Residency			
Taipei area	3 (50)	8 (72.7)	0.339
Northern	-	-	
Central	1 (16.70)	-	
Southern	-	1 (9.1)	
Gao-Ping area	2 (33.3)	1 (9.1)	
Eastern	-	1 (9.1)	

of foods and drinks that contain pathogens.²³ Lyme disease is a zoonosis with rodents or other small mammals (e.g., deer) as natural hosts. According to public health research released by the American Center for Disease Control and Prevention in August, 2015, the scale of Lyme disease infections has been increasing. The disease began in the northeast and upper midwest of the United States and has since spread; the cause of this spread remains unclear. However, the increasingly scattered distribution of forests may be one reason. When large forest areas undergo deforestation and woodlands are segmented into small pieces of land, they become favorable habitats for deer and small mammals, which are the most common hosts for ticks. Climate change can also increase the suitability of an environment for arthropods (including ticks) and can change the foraging times of hard ticks. Since 2007, Taiwan has had 17 imported cases of Lyme disease (11 from the United States), with an average of 0–3 annual cases. No high-risk group could be identified with respect to occupation; the occupational distribution among patients was scattered. The risk of Lyme disease is affected more by the distribution

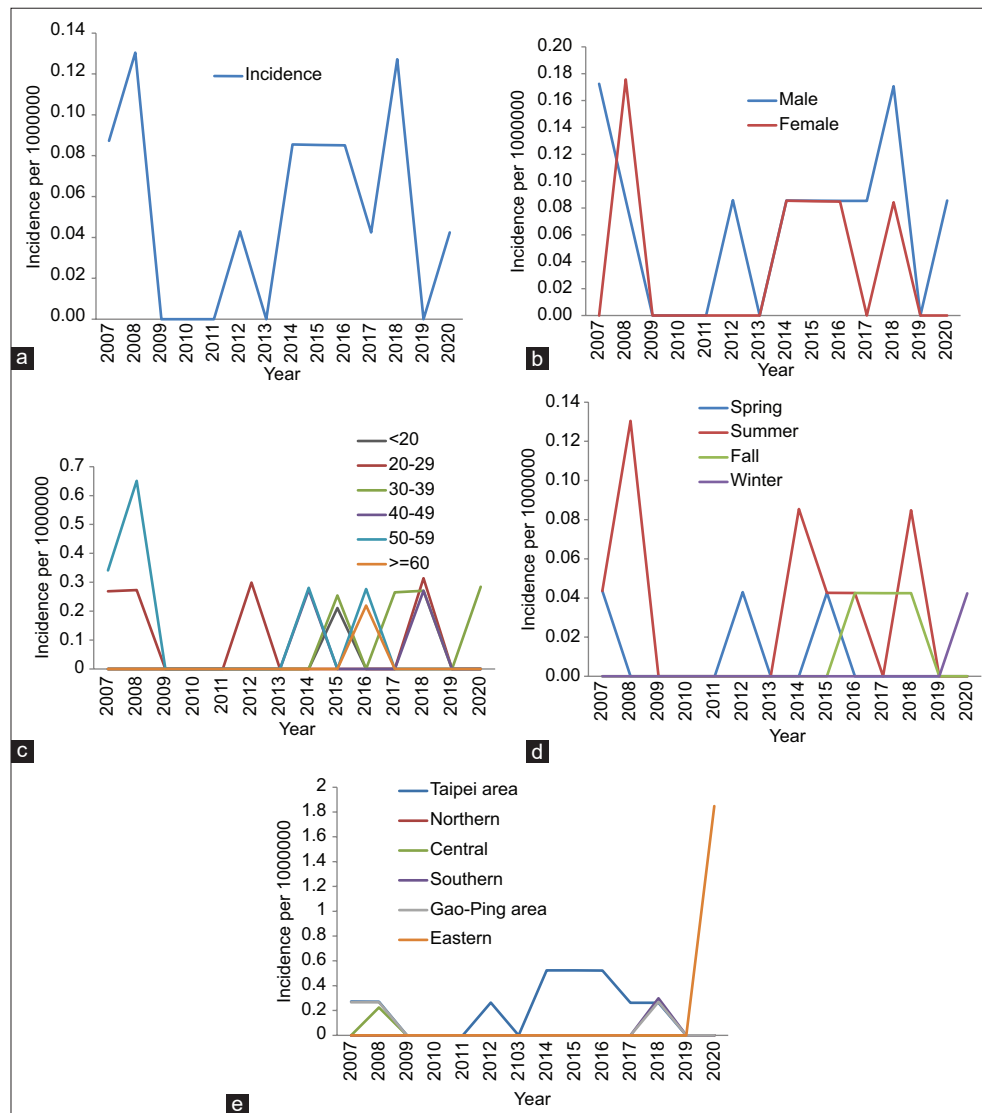


Figure 2: Confirmed Lyme disease incidence among patients in Taiwan according to (a) population, (b) sex, (c) age, (d) season, and (e) area of residence by year from 2007 to 2020

Table 3: Reported Lyme disease cases in Taiwan imported from the United States and other countries by year

Country	Year							
	2007-2008 (n=5)	2012 (n=1)	2014 (n=2)	2015 (n=2)	2016 (n=2)	2017 (n=1)	2018 (n=3)	2020 (n=1)
USA	4	1	1	1	1		2	1
Sweden					1		1	
Denmark	1							
England				1				
Germany			1					
Other						1		

of rodents or small mammals in an individual's daily living or leisure environments or the individual's direct or indirect exposure to *B. burgdorferi*. Because Taiwan is a travel hub in

East Asia, a popular tourist destination, and an active participant in international exchanges, it remains under the threat of imported Lyme disease from Western countries and areas in

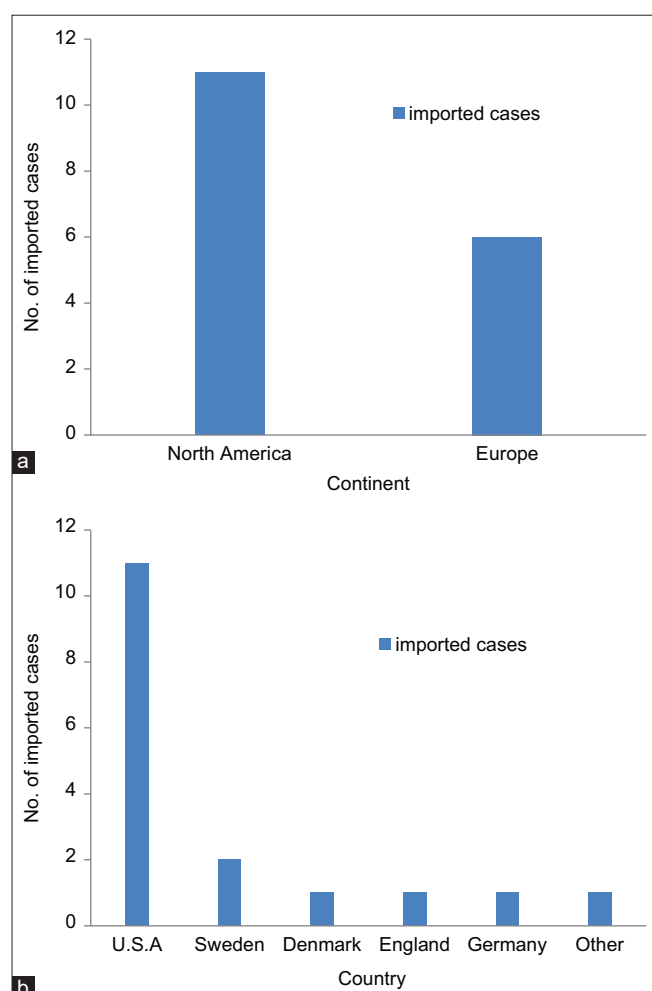


Figure 3: Lyme disease cases reported in Taiwan by (a) continent and (b) countries

which Lyme disease is epidemic (e.g., the United Kingdom, Germany, northern Europe, the United States, and Canada). The imported case of Lyme disease in 2020 involved an American man in his 30s who traveled to Taiwan with his family to visit relatives. He was quarantined following his arrival on November 27 and reported symptoms, including joint pain, fatigue, and bodily soreness, on December 1. On December 6, the medical authorities arranged a medical appointment for him. During the appointment, he told the doctor that he had been bitten by a tick in the United States. The hospital reported him as suspected of having a case of coronavirus-19 and Lyme disease; he tested negative for coronavirus-19 and positive for Lyme disease, which confirmed him as an imported case of Lyme disease.²⁴ To prevent imported cases from spreading Lyme disease and threatening public health, government health officials have expended considerable effort to enforce border quarantine at international harbors and airports, particularly on holidays with potential large crowds. The government has

also urged all inbound Taiwanese travelers to comply with fever screening procedures and report any symptoms they have experienced upon arrival, including fever, cough, vomit, diarrhea, skin rash, or jaundice, to quarantine staff. Foreign travelers who experience the aforementioned symptoms within 15 days of their arrival in Taiwan are recommended to seek immediate medical attention and to notify the doctor of their travel and contact history to enable early diagnosis and treatment and to prevent the spread of the disease.

In the United States, the age distribution of Lyme borreliosis is typically bimodal, with peaks among children aged 5–15 years and adults aged 45–55 years.²⁵ This was similar to our own results. In some European countries, such as Slovenia and Germany, the incidence of Lyme borreliosis is higher among adult women (55%) than among men (45%).²⁶ A previous study²⁷ indicated that the incidence of Lyme borreliosis is higher among men than among women in individuals <60 years old. However, the sex ratio is nearly equal or slightly higher in women in older age groups. A previous study also indicated that in the northeastern United States and in most of Europe, the peak months of disease onset are June and July because of the feeding habits of nymphal ticks.²⁶ These results were consistent with the present study finding that, in Taiwan, most Lyme cases had appeared in summer (June–August).

Lyme disease is a highly contagious bacterial disease and can be contracted by humans through the bite of *B. burgdorferi*-infected ticks. Because Taiwan, along with its offshore islands of Penghu, Kinmen, and Matsu, is a travel hub in Asia and has a warm, humid climate; dense population; and high human exposure to animals, it has conditions conducive to the spread of tick-borne diseases. The places people visit for work, business, and entertainment and the places they live may increase their exposure to vector ticks and thus the risk of Lyme disease. Although Taiwan has not recorded any domestic case of Lyme disease, a Taiwanese study successfully isolated *B. burgdorferi* from the skin biopsy specimens of patients with Lyme disease and conducted serological tests on the patients. In the study, *B. burgdorferi sensu stricto* and *Borrelia afzelii* were isolated from and identified in skin biopsies for the first time in Taiwan, highlighting the genetic diversity of *Borrelia* spirochetes among patients in Taiwan.²⁸ Another study reported the first case of detection and molecular identification of *Borrelia garinii* isolated from human skin in Taiwan.²⁹ A total of 273 serum specimens from different areas and sources were tested against *B. burgdorferi* antigens through enzyme-linked immunosorbent assay. The positive serological reaction rates were 3% in healthy individuals.²⁹ Accordingly, for all young patients who have been bitten by a tick, experienced erythema chronicum migrans, or developed

rheumatoid arthritis with unknown causes, potential Lyme infection should be considered.

Despite COVID-19-related disruptions in controlling Lyme disease, efforts need to be maintained to prevent vector-borne diseases during this pandemic.³⁰ Although travel restrictions brought a halt to global mobility and therefore also a substantial decline of imported and travel-associated Lyme disease, Lyme disease will become the most prevalent vector-borne disease again in travel medicine as soon as international travel resumes.

This study has two limitations. First, the information provided on the TCDC's TNIDSS is limited to basic epidemic data of patients with Lyme disease; no clinical data were available. Therefore, we failed to determine differences and trends in the patients' clinical data and symptoms. Second, the system did not provide any information of the genotype or strain of *B. burgdorferi*, and thus, we could not determine (1) the strains of *B. burgdorferi* that spread in Taiwan or (2) the phylogeny of the strains in Taiwan with those in other countries. Nonetheless, an advantage of this study is its access to the diverse digital data offered on the Internet platform (including those at its early stage of establishment) established by the Taiwanese public sector. This open platform has many years of data of considerable academic value in that they can be used for statistical analyses or by researchers and research institutions. However, the platform could expand its coverage of infectious diseases or other disease characteristics to further enhance its contribution to scientific research.

CONCLUSION

This study is the first in Taiwan to report the epidemic characteristics and trends of Lyme disease from 2007 to 2020. Subjects aged 50–59 years exhibited a gradual increase in incidence and a distinct pattern of seasonal variation (peak in summer). Furthermore, more imported cases involved men than women, and Taipei was a potential high-risk area. We recommend expanding Lyme disease self-protection programs for people older than 50 years to improve protection against the disease.

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Data availability statement

The data that support the findings of this study will be available in Taiwan CDC Database at <https://nidss.cdc.gov.tw/>, to allow for research findings

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Nil.

Conflicts of interest

There are no conflicts of interest.

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