

Epidemiology and risk factors for notifiable *Clostridium botulinum* infections in Taiwan from 2003 to 2020

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Abstract

Botulinum toxin is produced by *Clostridium botulinum*, a gram-positive anaerobic bacterium. This study aimed to examine the epidemiological characteristics, including sex, age, season in which infection occurred, place of residence, and epidemiological trends, of confirmed botulism cases in Taiwan from 2003 to 2020. This study examined the annual summary data on reported botulism in Taiwan's Center for Disease Control from 2003 to 2020 available to the public on the internet. We found that there were 50 confirmed domestic cases of botulism. The incidence of botulism ranged from 0 to 0.48 per 1000,000 from 2003 to 2020 and peaked in 2008 and 2010. During the 18-year investigation period in which 6-year intervals were used, the study results showed a decreasing trend (2003–2008, 2009–14, and 2015–2020, had 22, 19, 9 cases each). In terms of patients' gender, age, and place of residence, most of the patients were females (56%), were aged ≥ 50 years (48%), and resided in Taipei and northern Taiwan (44%). The number of botulism cases in Taiwan from 2012 to 2020 compared with other years (from 2003 to 2011) found that there were significant differences among patients within an age group of <20 years ($P = .003$, odds ratio = 18.500, and 95% confidence interval = 3.287–104.111), and there were significant differences among patients whose place of residence was Taipei metropolitan area ($P = .025$, odds ratio = 5.667, and 95% confidence interval = 1.248–25.734). During 2003 to 2009, there was no case of botulism among those aged <20 years. Over the last 10 years, botulism in children showed an increasing trend. A total of 9 children were found to have botulism during 2010 to 2020; most of these children were male (66.7%) and were infected during spring and summer (66.7%). This study is the first to report the number of confirmed domestic cases with botulism from surveillance data from Taiwan's Center for Disease Control during 2003 to 2020. This study also found that the place of residence and age were associated with an increased risk of botulism in Taiwan. This information may be useful for policymakers and clinical experts to direct prevention- and control-based activities regarding botulism that result in the most severe illness and the greatest burden on Taiwanese.

Abbreviations: CDC = Centre for Disease Control and Prevention, TCDC = Taiwan's Center for Disease Control.

Key words: botulism, *Clostridium botulinum*, domestic, epidemiology, retrospective, zoonosis

1. Introduction

There are sporadic cases of *Clostridium botulinum* infection worldwide. When food is prepared or stored, the spores that are not destroyed germinate and proliferate, producing toxins that cause familial or general botulism.^[1] Botulism rarely occurs following the consumption of commercially processed products unless there are defects in the manufacturing process, resulting in contamination and insufficient sterilization.^[2] Botulism has been reported in Asia, Australia, Europe, and

North and South America. The Centre for Disease Control and Prevention (CDC) has been monitoring cases of botulism in the United States since 1973. From 2011 to 2015, an average of 162 cases was reported annually; these primarily included infant botulism at 71% to 88%, followed by foodborne botulism, wound botulism, and botulism of unknown origin. Except for rare, large outbreaks, the total number of botulism cases has remained relatively stable over the past 10 years.^[3,4] Mortality resulting from botulism is low. The mortality rate has decreased significantly from over 60% in the 1950s to a

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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mere 3% in 2009. Most deaths reported are attributable to botulism of unknown origin, followed by foodborne, wound, and infant botulisms (<1%).^[5]

Botulinum toxin is produced by *C botulinum*, a gram-positive anaerobic bacterium.^[6] Eight distinct *C botulinum* toxin types have been described: A through H. Of these eight, types A, B, E, and rarely F, G, and H, cause human disease, whereas C and D cause disease in animals, such as cattle, ducks, and chickens. *C botulinum* toxin type H was first reported in 2014 and is the first new botulinum toxin type to be recognized in over four decades.^[7,8] Botulinum toxin is the most potent bacterial toxin and perhaps the most potent known poison. It is estimated that one gram of aerosolized botulinum toxin could kill at least one million people.^[9] The toxin itself has no smell or taste. If ingested, the toxin is primarily absorbed by the stomach and small intestine; the large intestine is capable of absorbing the toxin as well. The toxin is resistant to degradation by gastric acidity and human alimentary enzymes alike. When subjected to stress (e.g., starvation and low salt and sugar concentrations), and under specific environmental conditions (e.g., anaerobic environment and basic pH), *C botulinum* is able to form spores that are extremely resistant to environmental factors (e.g., temperature and chemicals) and can remain viable for many years.^[10] In contrast to the spores, the botulinum toxin is sensitive to high temperatures and common disinfectants; both heating to 85°C for 5 minutes^[11,12] or using a 0.1% hypochlorite solution^[13] are enough to degrade the toxin.

The production of botulinum toxins is attributable to improper food handling or storage, salted foods with insufficient acidity or alkaline foods, low-temperature sterilization of food, light salting of food without refrigeration (especially in sealed containers), and incomplete sterilization or insufficient cooking during canning of instant food. Under anaerobic conditions, *C botulinum* produces toxins, causing traditional (foodborne) botulinum poisoning after ingestion. The food items are mainly home-made pickled vegetables, fruits, fish, meat, sausages, or seafood. Foodborne botulism is caused by the ingestion of food contaminated by the preformed botulinum toxin. Toxin types A, B, and E have been associated with foodborne botulism.^[14,15] Moreover, *C botulinum* can infect wounds and subsequently produce neurotoxin in vivo. In theory, wound botulism should only be associated with puncture wounds, subcutaneous abscesses, and deep space infections, which provide the anaerobic environment required for spores to germinate and the organism to thrive. Recurrent wound botulism has occurred in some drug abusers using injections for drug administration.^[16]

Infant botulism occurs when *C botulinum* spores are ingested, colonize the host's gastrointestinal tract, and release toxin produced in vivo. In the United States, most cases are thought to result from the ingestion of environmental dust and soil containing *C botulinum* spores.^[11] Infant botulism involves infection between a period of 2 weeks and 1 year of age, and 88% of these patients are <6 months of age.^[17] There is no significant difference in race. Some adults with gastrointestinal problems might experience this disease. The neurological symptoms of foodborne botulism usually appear within 12 to 72 hours, with the shortest duration to onset being 2 hours and the longest duration to onset being 8 days.^[18] The shorter the incubation period, the more serious is the condition, and the higher is the mortality rate. The accurate incubation period of infant botulism is currently unknown. Botulism symptoms range from constipation, lethargy, fatigue, loss of appetite, drooping eyelids, difficulty swallowing, loss of head control, hypotonia, and general weakness, and the symptoms may sometimes progress to respiratory failure and death. This disease has a wide range of features and severity, ranging from mild to sudden death.^[19]

Taiwan is located at 23°4'N and 121°0'E and has a subtropical climate. The mean monthly temperature ranges from 16°C to 29°C, and the mean monthly relative humidity ranges from 75% to 90%. Taiwan is a developed country with a gross domestic

product per capita of 32,219 USD.^[20] Even though there have been no imported cases of *C botulinum* in recent years, local *C botulinum* infections are still reported in Taiwan,^[21] indicating that there may be a limited effectiveness of measures for limiting or controlling the disease. In Taiwan, there are both sporadic cases and clusters. However, there is little epidemiological information that utilizes big data to examine the risk of botulism in Taiwan. Therefore, this study aimed to use the Taiwan National Infectious Disease Statistics System to examine the epidemiological characteristics, differences, and trends of the number of local cases of *C botulinum* infection in the Taiwanese population based on sex, age, season, and area of residence during 2003 to 2020.

2. Methods

2.1. Ethical policy

Studies using information that is freely available in the public domain and that analyze open data sets where data have been properly anonymized do not require ethics approval. The authors are sure about the added value of this study that conforms with the public use of the government reports.^[22–24]

2.2. Definition of confirmed case and epidemiological survey^[25]

2.2.1. Definition of confirmed case Cases of foodborne botulism that were reported to the notifiable infectious diseases system from 2003 to 2020 and simultaneously met the clinical and laboratory test criteria.

- (1) Clinical criteria: patients with visual disturbance (blurred vision or diplopia), dysphagia, facial palsy, dry mouth, and other central nervous system symptoms, with limb weakness, respiratory failure, or gastrointestinal symptoms, and in whom botulism cannot be ruled out by the clinician.
- (2) Laboratory test criteria: *C botulinum* was isolated and identified from clinical samples (stools or vomitus), or the patients had a positive serum botulism toxin test result.

2.2.2. Laboratory diagnostic method

- (1) Serum test: The patient's serum was used for animal toxicity testing, wherein a mouse was injected with the patient's serum and was observed for classical botulism symptoms, such as dyspnea, limb weakness, typical abdominal breathing, or even respiratory paralysis, failure, or death within 24 hours of injection. If the mouse showed classical botulism symptoms, the antitoxin for botulism toxins A, B, E, and F was further injected and an animal neutralization test was performed to identify the type of toxin.
- (2) Other tests: Anaerobic culture was performed, and the supernatant was collected after 3 days for the aforementioned animal experiments. The pellet was used for bacterial culture, isolation, and identification. The purified *C botulinum* strain was used for further animal experiments.

2.2.3. Epidemiological survey and control measures After Taiwan's Center for Disease Control (TCDC) received a case notification, it immediately sent antitoxin for treatment to the hospital where the patient was admitted while simultaneously performing epidemiological investigations to assess epidemic severity within the shortest time and assist in the identification of potentially contaminated foodstuffs. Besides recording the disease course, symptoms, and treatment in the epidemiological survey, the incubation period for botulism (12–36 hours)

was used as a reference, and the patient's food record from 3 days preceding the disease onset, including type of foodstuff consumed, storage conditions, processing method, whether family members shared the food, and amount of food consumed after determining the correct time of disease onset of the patient or his/her family members, was obtained. If many people shared the same food, they were interviewed one by one and cross-comparison was carried out to obtain the most complete food record.

2.3. Data source

This study used TNIDSS, a public database established by TCDC.^[26] The public TNIDSS database includes data on five categories of communicable diseases listed in the Communicable Control Act literature. The website is updated with the latest epidemic information early each morning, providing the latest charts (e.g., run charts), reports (in Excel format), distributions (in county, city, or township), and encyclopedias of different disease types. This allows for epidemic-based information to become more transparent and up to date. To ensure information security and privacy, the public database includes only secondary data (i.e., notification date, onset date, confirmation date, and the number of confirmed domestic and imported cases of *C botulinum* infections) without case details. The database does not contain the medical history of patients, their signs and symptoms, or the results of laboratory testing.

2.4. Data analysis

This is a retrospective study of all domestic *C botulinum* infection cases since 2003. We confirmed the number of people diagnosed as having *C botulinum* infection from 2003 to 2011 and from 2012 to 2020 and examined the distribution of their epidemiological characteristics (sex, age, time of diagnosis, and living area), differences, and results. Next, we reported the sex, age, time of diagnosis, residential area change, trends, and related results in our analysis of the cases of *C botulinum* infections from 2003 to 2008, from 2009 to 2014, and from 2015 to 2020. Descriptive data are shown as mean 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 Ltd., Taipei, Taiwan). All statistical tests were 2-sided with an α value of 0.05. *P* values of <.05 were considered to represent statistical significance.

3. Results

3.1. Epidemiological features

During the study period, 50 children and adults (Table 1), 28 (56.0%) of which were female, were confirmed as having the disease. Among them, 9 (18%) patients were <19 years old, 29 (58.0%) were 20–59 years old and 12 (24.0%) were ≥60 years old. A total of 23 patients were infected in spring, 11 in summer, 5 in fall, and 11 in winter, and all patients were examined and screened for *C botulinum* infections. The characteristics of the confirmed cases (including residence) are shown in Table 1. In the comparison of cases reported between 2003–2011 and 2012–2020, differences in sex ($P = .669$) and season of confirmation ($P = .257$) were non-significant, whereas a significant difference in age groups ($P = .003$) and place of residence ($P = .025$; Table 2) was observed. In the comparison among spring, summer, fall, winter in terms of the cases of botulism reported between 2003 and 2020, differences in sex ($P = .222$), age groups ($P = .808$), and place of residence ($P = .498$; Table 3) were non-significant. In the comparison among Taipei, northern, central, southern, Gao-ping, and

eastern areas in terms of the cases of botulism between 2003 and 2020, non-significant differences in sex ($P = .225$) and age groups ($P = .652$; Table 4) were observed. In the comparison among male and female cases of botulism between 2003 and 2020, differences in age groups were non-significant ($P = .284$; Table 5). In this study, nine children were infected with botulinum (Table 6).

3.2. Epidemic curve

During the study period (January 2003–December 2020), 50 confirmed domestic cases were reported (Fig. 1A), of which the incidence rate was reported from 2003 to 2020 (Fig. 1A). Botulism was detected during 2003 to 2008 (44.0% [22/50]), 2009 to 2014 (38.0% [19/50]), and 2015 to 2020 (18.0% [8/21]); Figure 1B. Botulism was reported in males and females during 2003 to 2008 (14.0% [7/50]; 30.0% [15/50], respectively), 2009 to 2014 (20.0% [10/50]; 18.0% [9/50], respectively), and 2015 to 2020 (10.0% [5/50]; 8.0% [4/50], respectively; Fig. 1C). Botulism was detected in the age range of <20 years and ≥50 years in 2003 to 2008 (0% [0/50]; 28.0% [14/50], respectively), 2009 to 2014 (8.0% [4/50]; 12.0% [6/50], respectively), and 2015 to 2020 (10.0% [5/50]; 8.0% [4/50], respectively; Fig. 1D). Botulism was detected in the spring and summer seasons in 2003 to 2008 (22% [11/50]; 2.0% [1/50], respectively), 2009 to 2014 (20.0% [10/50]; 14.0% [7/50], respectively), and 2015 to 2020 (4.0% [2/50]; 6.0% [3/50], respectively; Fig. 1E). Botulism was detected in the Taipei and northern areas of residency during 2003 to 2008 (6.0% [3/50]; 8.0% [4/50], respectively), 2009 to 2014 (6.0% [3/50]; 14.0% [7/50], respectively), and 2015 to 2020 (10.0% [5/50]; 0% [0/50], respectively; Fig. 1F).

4. Discussion

Recent related papers^[27–32] have reported the presence of the toxin in family canned plant foods (such as asparagus, garlics), family foods (such as potatoes, concentrated soup, sausages, and spicy sauces), raw vegetable salads made in hotels, and

Table 1
Demographic characteristics of the patients confirmed as having botulism in Taiwan from 2003 to 2020.

Variables	Domestic cases	
	N = 50	%
Sex		
Male	22	44
Female	28	56
Age		
<20	9	18
20–29	6	12
30–39	5	10
40–49	6	12
50–59	12	24
>60	12	24
Season		
Spring	23	46
Summer	11	22
Fall	5	10
Winter	11	22
Residency		
Taipei area	11	22
Northern	11	22
Central	12	24
Southern	7	14
Gao-Ping area	8	16
East	1	2

Table 2
The epidemiological features of botulism cases from 2003 to 2020.

Variables	Year		P value
	2003–2011	2012–2020	
Sex			
Male	17	5	.669
Female	23	5	
Age			
<20	3	6	.003
20–29	6	0	
30–39	5	0	
40–49	6	0	
50–59	11	1	
>60	9	3	
Season			
Spring	21	2	.257
Summer	7	4	
Fall	4	1	
Winter	8	3	
Residency			
Taipei area	6	5	.025
Northern	10	1	
Central	12	0	
Southern	5	2	
Gao-Ping area	7	1	
East	0	1	

commercially available carrot juice in Europe and USA. Apart from the consumption of traditional canned foods that are sold in the market, the consumption of any home-made canned food, food that is weakly acidic or a neutral pH (pH 5–7), and food with low salinity (0.1%–5.0%) stored at low temperatures without thermal processing may pose a risk of botulism.^[33] In addition botulism cases have often occurred in China owing to the consumption of smelly tofu, douchi, fermented chili bean paste, fermented bean curd, and other fermented bean products, salted fish, sausages, and salted duck eggs,^[34–37] indicating that all foodstuffs may cause botulism. Due to differences in customs and dietary culture, botulism may be caused by different types of botulism toxin. For example, native Americans in Alaska developed type E botulism owing to the consumption of fermented

fish and fish eggs.^[14] In 1987, 1990, 2006, and 2008, type B botulism occurred in mountainous tribes in Nantou, Yilan, and Miaoli counties in Taiwan after people consumed preserved Reeves's muntjac, mountain goat, or bird meat.^[14,38,39] However, most cases of botulism in Taiwan in recent years have been type A, and the proportion of type B cases is very low. Foodborne botulism is a public health emergency. Therefore, we recommend that clinicians in medical institutions should be vigilant in reporting and working closely with the disease prevention and control and food hygiene authorities to achieve early diagnosis and treatment and identify possible infection sources to prevent outbreaks from occurring.

The examination of the epidemiological data of the confirmed botulism cases from 2003 to 2020 in this study found that the number of cases in 2012 to 2012 (20%, 10//50) was drastically decreased compared to that in 2003 to 2011 (80%, 40//50), indicating that Taiwan's healthcare and public health education and advocacy quality is similar to that of the healthcare and public health education and advocacy of developed countries. In addition, this study found that the highest incidence occurred in 2008 and 2010. We speculated that the main reason for this was that there were many clusters in these 2 years, resulting in a large increase in cases.

Examination of the overall data indicated that there were more cases in females than in males, in people aged < 20 years and ≥50 years, in the season of spring compared to that in other seasons, and in populations residing in Taipei and northern Taiwan, which have a higher risk of developing botulism. The results of this study were similar to the findings of literature from other countries.^[17,40,41] Our study also found that the risk of developing botulism in the <20 years age group in the last 9 years (2012–2020) was 18.5 times than in the preceding 9 years (2003–2011; odds ratio = 18.5), which is similar to the findings of literature from other countries.^[42] Our study also found that there was a decreasing trend in the age of onset during 2003 to 2020, which reported a decreased from 50 to 59 years (27.5%; 11/40) to <20 years (60%; 6/10). This study indicated that more elderly females are infected by *C botulinum*. We suggested that the increase in botulism cases for elderly females might be due to the fact that elderly women have been staying at home for a long time and cooking food. Therefore, this study inferred that the <19 years age group may be a high-risk factor for developing botulism at present. Furthermore, the risk of developing botulism in residents from

Table 3
The association of season with sex, age, and area of residence based on a survey of confirmed cases of botulism between 2003 and 2020 in Taiwan.

Variables	Season				P value
	Spring	Summer	Fall	Winter	
Sex					
Male	11	7	2	2	.222
Female	12	4	3	9	
Age					
<20	3	3	1	2	.808
20–29	4	1	0	1	
30–39	0	1	1	3	
40–49	3	2	1	0	
50–59	6	2	1	3	
>60	7	2	1	2	
Residency					
Taipei	3	2	3	3	.498
Northern	8	1	0	2	
Central	5	3	1	3	
Southern	1	3	1	2	
Gao-Ping	5	2	0	1	
East	1	0	0	0	

Table 4

The association of area of residence with sex and age based on a survey of confirmed cases of botulism between 2003 and 2020 in Taiwan.

Variables	Residency						P value
	Taipei area	Northern	Central	Southern	Gao-Ping area	East	
Sex							
Male	7	2	6	2	4	1	.225
Female	4	9	6	5	4	0	
Age							
<20	3	2	1	1	1	1	.652
20–29	2	0	1	1	2	0	
30–39	2	0	2	1	0	0	
40–49	0	3	2	1	0	0	
50–59	3	3	4	1	1	0	
>60	1	3	2	2	4	0	

Table 5

The association between sex and age based on a survey of confirmed cases of botulism between 2003 and 2020 in Taiwan.

Variables	Sex		P value
	Male	Female	
Age			
<20	6	3	.284
20–29	4	2	
30–39	3	2	
40–49	2	4	
50–59	4	8	
>60	3	9	

Table 6

The epidemiological features of child with botulism observed in this study from 2003 to 2020.

Year	Age	Sex	Season	Residency
2010	15–19	Male	Spring	Northern
2010	15–19	Male	Spring	Central
2011	4	Male	Summer	Gao-Ping area
2013	10–14	Female	Summer	Northern
2015	<1	Female	Winter	Southern
2016	15–19	Male	Spring	East
2016	10–14	Male	Fall	Taipei area
2016	10–14	Female	Winter	Taipei area
2020	<1	Male	Summer	Taipei area

the Taipei metropolitan area during 2012 to 2020 was 5.7 times (odds ratio = 5.7) that of the preceding 9 years (2003–2011). Therefore, this study inferred that residing in Taipei may be a high-risk factor for developing botulism at present. Understanding the people, time, and place of cases, incidence, or trend variations (direction) in infectious diseases epidemiology may help government health institutions and public health professionals or epidemiological experts to rapidly react to disease and promptly determine the infection sources of botulism, and block transmission and prevent subsequent epidemics from occurring.

Infant botulism is defined as a neuroparalytic disease that can endanger children aged below 12 months.^[43] When infants consume food contaminated with *C botulinum* spores,^[44–46] the bacteria can proliferate in the gut and produce toxins as their immune system and gut microbiota are not well developed.^[47–49] During this study period, a medical center in Taiwan reported

a case of botulism in a 5-month-old female infant in January 2015.^[50] This female infant did not have any congenital disease, had complete vaccination history, and normal nervous development. After birth, she was breastfed, and her daily appetite and activity were good. She did not consume honey or canned food and did not travel overseas. Her initial symptoms include poor appetite, constipation, generalized weakness, weak cry, fever, tachycardia, and shortness of breath. During hospitalization, the infant's face was expressionless, and corneal irritation, vomiting, and cough reflex had disappeared. She had dysphagia and required saliva suction and nasogastric tube feeding. Peristalsis disappeared and limb and neck weakness were present. Based on sample test results, food test results, and disease course changes, the clinician diagnosed her with infant botulism type A. This case was the first reported case of infant botulism in the last 10 years in Taiwan, but the test results of 5 suspected foodstuffs were negative and the infection source was unclear. A case of botulism case in 2020 was that of a 4-month-old male infant in northern Taiwan who consumed home-made baby food in mid-June. At the end of June, he developed constipation, poor appetite, tachypnea, and fever. His family members sent him to the hospital for treatment. During hospitalization, he successively developed tachycardia, limb weakness, decreased deep tendon reflex, and drooping eyelids. The hospital collected samples and notified authorities of a case of suspected botulism. After testing, type B *C botulinum* was identified in stool samples. According to literature from other countries, *C botulinum* spores are ubiquitous in soil/dust or agricultural products.^[51] During food manufacturing, if cleaning, sterilization, and heating are insufficient, bacteria and spores tend to contaminate foodstuffs. Therefore, we recommend that food should be boiled for at least 10 minutes and stirred; canned foods with bulging lids should not be consumed; and canned foods with foul odors after opening should not be consumed. Furthermore, as *C botulinum* spores have a broad distribution in nature, education and advocacy should be provided on avoiding the consumption of honey by infants <1 year and the thorough cleaning and peeling of vegetables and fruits as unpeeled vegetables and fruits may be contaminated with soil containing spores. In addition, our study analysis of botulism patients <19 years found that there were 9 children, of which most cases were male (66.7%, 6/9). This was significantly different from the phenomenon of more female patients in the adult population (60.9%, 25/41). We inferred that the risk of developing botulism is higher in males; the prevalence of pediatric population is higher in spring and summer (66.7%, 6/9), which means that seasonal influence is a critical factor affecting botulism when parents or their family members care for children. Furthermore, our study found that there was no botulism case <19 years in 2003 to 2009, but cases occurred from 2010 onwards and reached a peak in

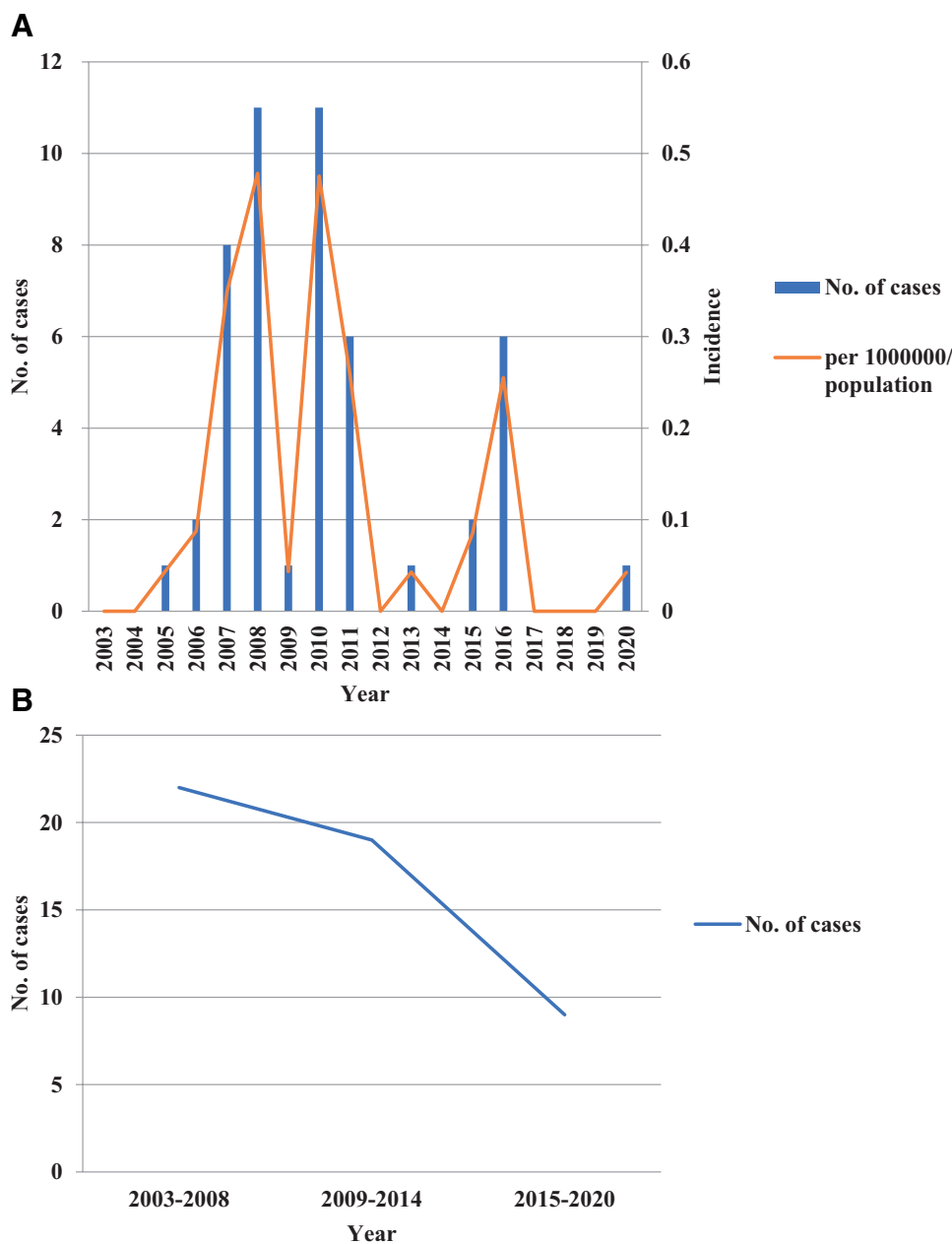


Figure 1. The number of confirmed cases of botulism in Taiwan according to (A) incidence case, (B) year, (C) gender, (D) age, (E) season, and (F) area of residence based on the year from 2003 to 2020.

2016, which showed that botulism in children is a major public health issue in Taiwan. Government health departments should actively propose effective control measures to prevent epidemics from occurring and safeguard children's health.

In recent years, the number of cases of iatrogenic botulism has gradually increased owing to the widespread use of the botulinum toxin in medical practice. As an injection of the toxin for cosmetic purposes is a medical procedure with high risk, individuals should carefully assess health needs and medical risks before undergoing this procedure. During the studied period, a 40-year-old woman underwent the cosmetic procedure overseas in October 2018. After several days, she developed dysphagia, blurred vision, and labored breathing. In November of the same year, the clinician assessed her and notified the CDC that the patient was a suspected case of botulism.^[52] Therefore, we recommend that people undergoing cosmetic procedures undergo the same in qualified and registered medical institutions, and the physician performing the procedure should be a qualified

medical staff. The public are recommended to inspect the exact components of the injection and the health-authority license to avoid harming the public's health. If a clinician encounters a patient who is suspected of developing botulism after receiving a botulinum toxin injection, the clinician should notify the relevant authorities.

The largest botulism cluster in Taiwan occurred in September 1986 when a printing factory employee in Changhua county consumed preserved peanuts produced by an unlicensed family-run factory; this was the first botulism cluster in Taiwan with complete records. At that time, 9 patients consumed preserved peanuts produced by an unlicensed family-run factory, resulting in 9 cases of type A botulism and 2 deaths. Epidemiological investigations speculated that spores entered the cans and germinated, resulting in contaminated food and botulism.^[53] In 1986, the health authority of Taiwan promulgated the "Hygiene standards for low-acidity canned food manufacturing, flavoring, and processing sites and facilities" according to the Act

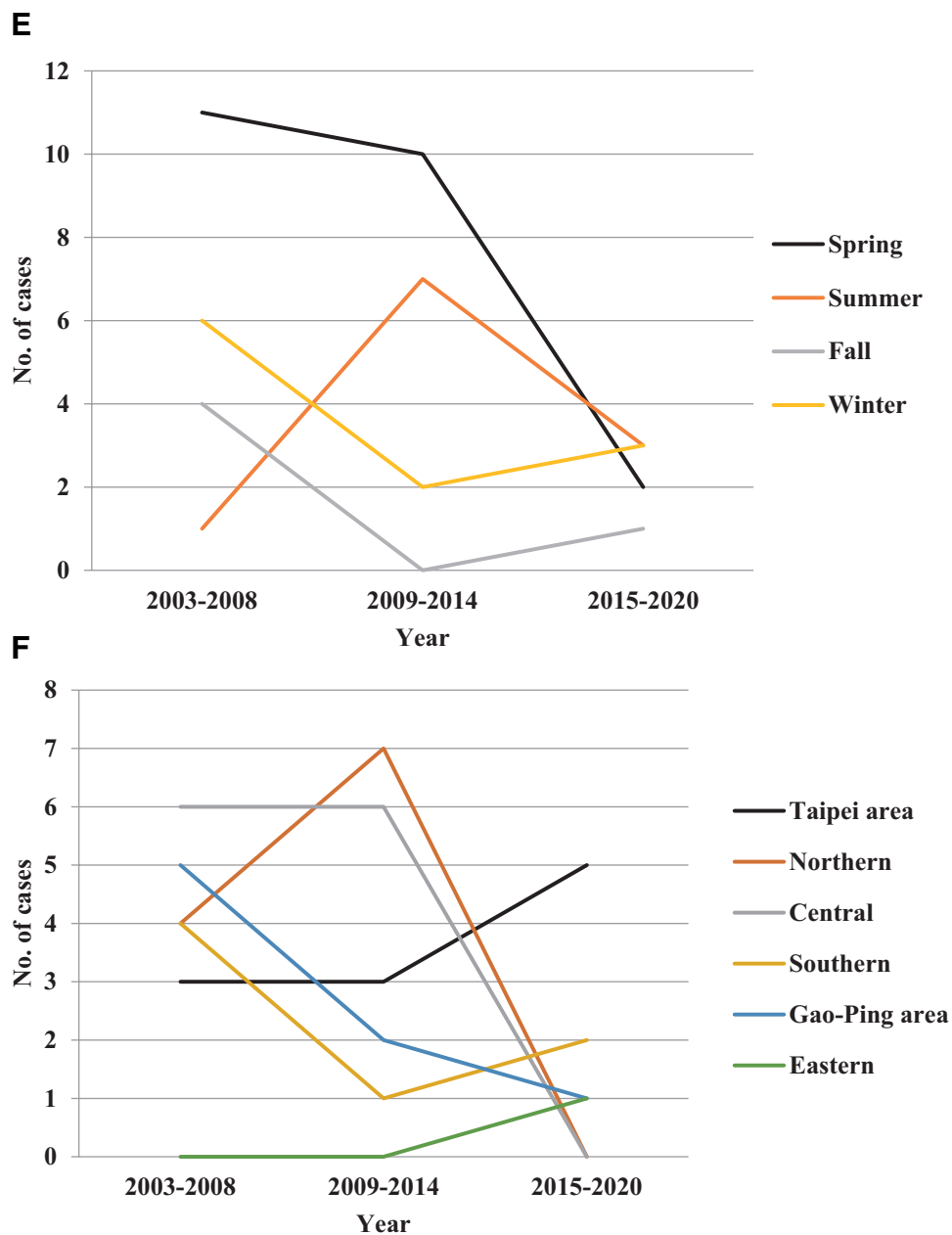


Figure 1. Continued

Governing Food Safety and Sanitation and established a locally produced low-acidity canned food inspection and registration system. In 1989, the government announced that for commercial sterilization, the sterilization process must achieve commercial sterility and the sterilized canned foods should be free from microbial re-proliferation when stored at room temperature without refrigeration, and live microorganisms or spores that can endanger human health should be absent. Since then, botulism cases that occurred owing to the consumption of canned foods are rare in Taiwan. During the study period, in February 2008, the health authority received notifications regarding two cases of suspected botulism from primary medical institutions and carried out epidemiological surveys. The results found that the two patients were sisters who stayed together and had clinical symptoms of classical botulism. After investigation and the collection of blood and stool samples as well as food samples from foods shared by both the patients, a botulinum toxin (type A, B, and E) test was performed. Results showed that the type A botulinum toxin was detected in the serum of both the patients

but not in the food samples. Based on person, time, and place correlation in epidemiology and the laboratory test result of the same botulinum toxin, this was considered to be a family cluster of type A botulism. Previous studies speculated that as the diagnosis and notification of the aforementioned inpatient case was performed on Day 6 of disease onset, as disease symptoms may cause the patient to be unable to recall her food record during the incubation period, or owing to the absence of remaining food for sampling, the integrity of food samples collected as affected and may be the main reason why the causative food was not confirmed. The local health authorities had carried out necessary food hygiene and safety measures, such as preventive sealing of the same batch of products and counseling for improvement of food processing. Subsequently, no related cases occurred.^[54] In addition, a Taiwanese study reported confirmed cases from 2007 to 2009, samples tested were mostly type A *C botulinum*, and the suspected foods were soybean products consumed before disease onset, which was a possible risk factor.^[55] In addition, a previous Taiwanese study^[56] reported that among

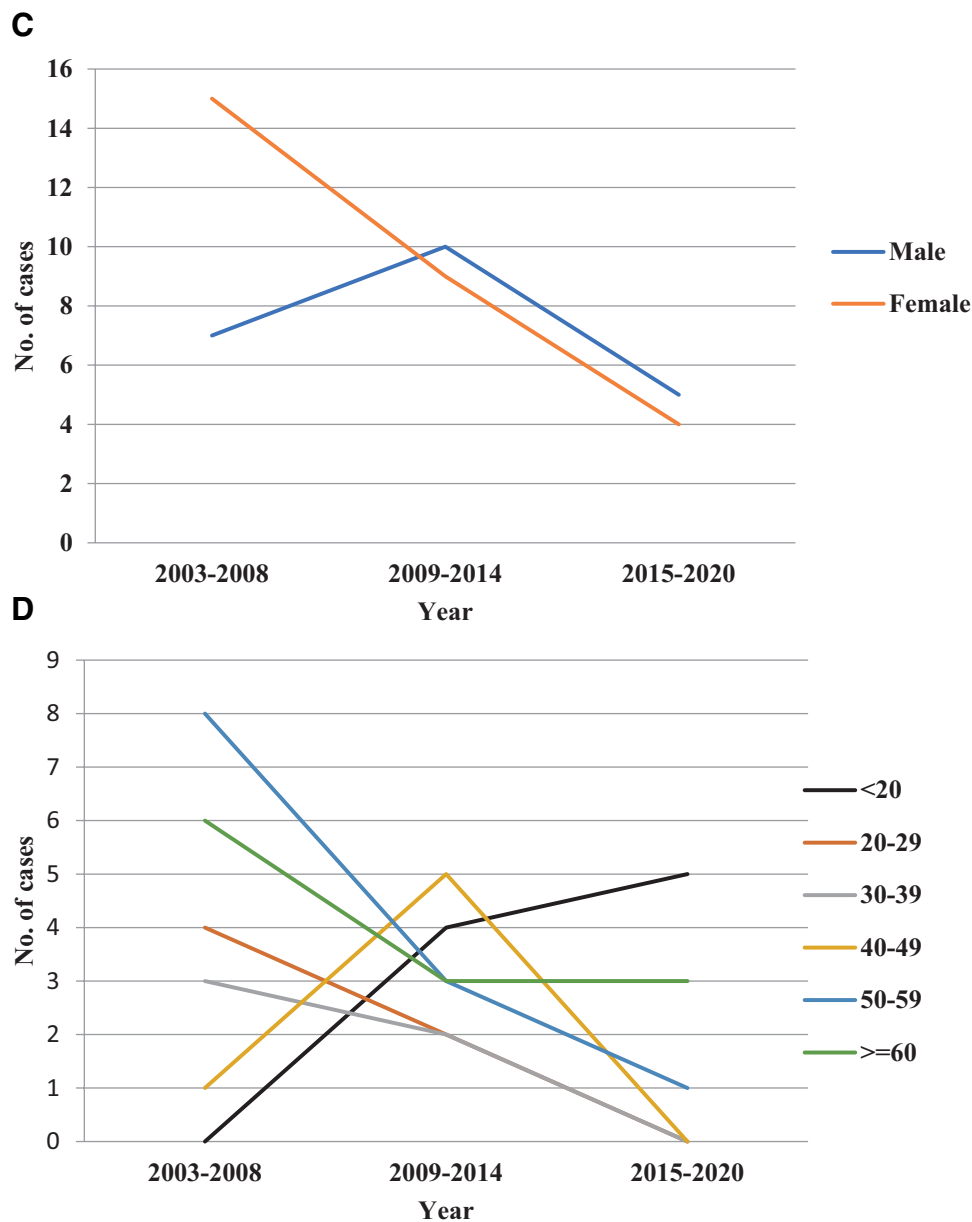


Figure 1. Continued

the suspected cases in the notifiable infectious disease system, 9 cases had met the clinical and laboratory test criteria and were confirmed as foodborne botulism cases, including 2 clusters and 4 sporadic cases. Epidemiological surveys found that the cases in the clusters had previously consumed vacuum-packed ready-to-eat food during the incubation period. The health authorities collected samples from the homes of these cases, but there was no residual food for sampling in most cases, and direct evidence for suspected food contamination was not found. This showed that the dietary factor for botulism is relatively complex. Therefore, this study recommends that when disease control staff participate in an investigation in the future, they should discard old concepts of only following up on canned foods as the processing, storage, and transportation of any food stuff may be the cause of botulism. In-depth analysis of the sources of condiments should also be carried out. The storage condition of the foods or meals should be recorded clearly, and samples of suspected foodstuffs should be properly stored. The infectious diseases investigation system of the government health authority should also include soybean products to the list of suspected

foodstuffs to facilitate evaluation by disease control staff and determine the toxin source and block transmission as soon as possible.

Our study has the following 2 limitations. First, the basic epidemiological information of *C botulinum* infection the patients provided in the infectious disease statistical data on the Taiwan CDC website does not contain clinical data. Therefore, we were unable to compare the differences or trends in clinical data or symptoms between patients. 2. The information on this platform did not contain *C botulinum* genotype or strain-related information. Therefore, we were unable to determine which *C botulinum* strains were circulating in Taiwan or the phylogenetic relationship between Taiwanese strains and strains from other countries. However, our study has 2 distinct advantages. To the best of our knowledge, this study is the first to report the number of confirmed domestic cases with botulism from surveillance data from TCDC during 2003 to 2020. The level of data informatization on the existing website of Taiwan government departments (including the initial stage of construction) is high. This public platform stores many years of data, allowing

researchers or institutions to be able to carry out statistical or data analyses or fully utilize its academic value, and surveillance of infection type or other characteristics should be increased so that the knowledge obtained via scientific research can continue to increase.

This study is the first to report the epidemiological characteristics and trends of *C botulinum* infections in Taiwan from 2003 to 2020. In this study on the incidence of *C botulinum* infections in Taiwan, subjects aged ≥ 50 years exhibited a gradual increase in incidence and a distinct pattern of seasonal variation (peak in spring). Moreover, more females were local cases than males, and a risk factor in terms of area of residence might be living in Taipei and northern areas of Taiwan, patients with <20 years old age group or elderly females. Furthermore, this study highly recommended providing knowledge regarding self-protection from *C botulinum* infections to people >50 years of age for better protection against the disease. Furthermore, in recent years (2010–2020), there has been a gradual increase in the number of children with botulism. Such information will be useful for policymakers and clinical experts to direct prevention and control activities for *C botulinum* infections that cause the most severe illness and the greatest burden on Taiwanese. This study highlights the importance of studies with prolonged study durations and those covering geographically vast areas, particularly for pathogens with variable characteristics and their reservoirs to understand the implications of the transmission of zoonotic diseases in human populations.

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