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Severe Systemic Reactions Following Bee Sting Injuries in Korea

Ji Hwan Lee, Min Joung Kim, Yoo Seok Park, EungNam Kim, Hyun Soo Chung, and Sung Phil Chung
Department of Emergency Medicine, Yonsei University College of Medicine, Seoul, Korea.

Purpose: Most bee sting injuries are benign, although sometimes they can result in life threatening outcomes, such as anaphylaxis and death. The purpose of this study was to investigate the epidemiologic status of bee sting injuries in Korea and to identify risk factors associated with severe systemic reactions (SSRs).
Materials and Methods: Cases were extracted from a multicenter retrospective registry for patients who had visited emergency departments (EDs) for bee sting injuries. SSRs were defined as hypotension or altered mental status upon ED arrival, hospitalization, or death. Patient demographics and injury characteristics were compared between SSR and non-SSR groups. Logistic regression was performed to identify risk factors for bee sting-associated SSRs, and the characteristics of fatality cases were summarized.
Results: Among the 9673 patients with bee sting injuries, 537 had an SSR and 38 died. The most frequent injury sites included the hands and head/face. Logistic regression analysis revealed that the occurrence of SSRs was associated with male sex [odds ratio (95% confidence interval); 1.634 (1.133–2.357)] and age [1.030 (1.020–1.041)]. Additionally, the risk of SSRs from trunk and head/face stings was high [2.858 (1.405–5.815) and 2.123 (1.333–3.382), respectively]. Bee venom acupuncture [3.685 (1.408–9.641)] and stings in the winter [4.573 (1.420–14.723)] were factors that increased the risk of SSRs.
Conclusion: Our findings emphasize the need for implementing safety policies and education on bee sting-related incidents to protect high-risk groups.

Key Words: Hymenoptera, insect sting, emergency departments, risk factors

INTRODUCTION

Approximately 12000 patients experience bee stings annually in Korea.[1] The number of emergency calls for beehive removal in residential areas increased from 60000 in 2010 to 120000 in 2014. Accordingly, the number of patients who visited hospitals for bee stings also increased from 12000 to 22000 in the same period.[2]

In Korea, 30 bee species are known to be distributed in the *Vespidae* family.[3] People are usually not stung by honeybees, and medical treatment is rarely sought due to minor effects. Therefore, it is likely that most bee stings cases are elicited by wasp stings. The most common wasps identified from digital images of removed nests are *Polistes rothneyi koreanus* and *Vespa velutina nigrithorax*.[2,4]

The response to a hymenopteran sting can be classified into four categories: 1) local reactions, such as swelling and pain at the sting site; 2) uncomplicated allergic reactions; 3) anaphylactic reactions causing bronchial constriction and shock; and 4) direct systemic toxic reactions.[5] A systemic toxic reaction occurs when a large amount of venom is injected into the body following multiple stings and may cause acute renal failure, hemolysis, hepatic injury, and possibly even death.[6] Previous studies have focused on anaphylactic reactions; however, there are few studies on the characteristics of patients treated in an emergency department (ED) after bee stings.[7-9]

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Corresponding author: Sung Phil Chung, MD, PhD, Department of Emergency Medicine, Yonsei University College of Medicine, 211 Eonju-ro, Gangnam-gu, Seoul 06273, Korea.
E-mail: EMSTAR@yuhs.ac

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Understanding the epidemiology of patients with bee stings who have been treated in the ED and the risk factors associated with life-threatening reactions will provide valuable information with which to screen and prioritize patients according to associated risk. Therefore, the purpose of this study was to investigate the epidemiological characteristics of bee sting injuries based on data collected from Korean EDs and to identify the risk factors contributing to severe systemic reactions (SSRs) following bee stings.

MATERIALS AND METHODS

Study design

This was a retrospective cohort study using data from the ED-based Injury In-depth Surveillance (EDIIS) project hosted by the Korea Disease Control and Prevention Agency (Cheongju, Korea). The EDIIS is a multicenter, prospective registry of data related to injuries caused by external factors, such as trauma, poisoning, or environmental injury, collected from 23 EDs in Korea. This study was approved by the Severance Hospital Institutional Review Board (4-2022-0182) and exempted from requiring informed consent from the patients due to the retrospective nature of the study.

Inclusion criteria and variables

Patients with their "main materials causing injury" recorded as "bee, hornet, and bumblebee" were extracted from the EDIIS database during January 2011–December 2019. Demographic characteristics and information related to circumstances of the injury and its severity were collected. The anatomical site of the injury was classified into head/face, neck, trunk, hands, arms, feet, legs, and two or more sites based on the diagnostic codes. The locations where bee stings occurred were classified into residential area, public area, educational facilities, industrial/construction sites, and other outdoor places. The types of activities at the time of injury were categorized into daily, sport, occupational, educational, leisure, and other activities. The "others" category was treated as missing information because a specific type of activity could not be suggested. The seasons were defined as March–May for spring, June–August for summer, September–November for autumn, and December–February for winter. A special type of intentional bee sting was categorized as the apitherapy group (e.g., bee venom injected into the body with the therapeutic purpose of reducing musculoskeletal pain and inflammation).[10] The outcome variable was SSR and was defined as one or more of the following: systolic blood pressure <90 mm Hg or altered mental status (Glasgow coma scale <15) at ED arrival or when the result of ED treatment was hospitalization or death.

Statistical analysis

Categorical variables are presented as numbers (%) and continuous variables as medians (interquartile range) because the data did not follow a normal distribution. The chi-square and Mann–Whitney U test were used to compare non-SSR and SSR groups. Uni- and multivariable logistic regressions were performed to identify factors contributing to the occurrence of SSRs, with results are presented as odds ratios (OR) with 95% confidence intervals (CI). Variables with $p<0.05$ in univariable analysis were selected for further multivariable analysis. SPSS statistics (version 26.0, IBM Corp. Armonk, NY, USA) was used for statistical analysis, and statistical significance was set at $p<0.05$.

RESULTS

A total of 1669280 injured patients were treated at 23 EDs during the study period. Among them, 9673 patients were identified as having bee sting injuries and 537 (5.6%) were included in the SSR group, which consisted of 147 altered mental status, 260 hypotensive, 266 hospitalized, and 38 mortality cases.

Characteristics of bee sting injuries

Basic demographic characteristics of the patients are presented in Table 1. The proportion of men and median age were higher in the SSR group than in the non-SSR group ($p=0.010$ and $p<0.001$, respectively). The number of patients decreased as age increased until the age of 15, after which it again increased steadily from 16 to 51–60 years and subsequently decreased (Fig. 1). Over 90% of bee sting injuries occurred in the summer and autumn, with 55.1% occurring in August and September. Subsequently, the incidence decreased sharply, with fewer than 100 cases per month between December and March (Fig. 2). The proportion of patients stung in the winter was higher in the SSR group than that in the non-SSR group ($p<0.001$). The annual incidence rate of bee stings did not differ between the two groups.

Injury characteristics of the patients are presented in Table 2. Other outdoor places (67.6%) and daily activities (54.7%) were the most frequent location and type of activity at the time of the stings. The most frequent anatomical site of stings was the hands (28.5%), followed by the head and face (20.9%). The number of injuries occurring at two or more sites was 15.0%. The proportion of patients stung in other outdoor places and industrial/construction sites was higher in the SSR group than in the non-SSR group ($p<0.001$). The most frequent injury site was the hands in the non-SSR group, whereas it was the head and face in the SSR group ($p<0.001$). Among patients with a known injury mechanism, 1.4% (83/6031) were identified as being injured during apitherapy. Of these, 12 patients (14.5%) were classified into the SSR group, and the proportion of apitherapy cases was higher in the SSR group than in the non-SSR group ($p=0.002$).

Table 1. Comparison of Patient Demographics between the SSR and Non-SSR Groups

	Total (n=9673)	Non-SSR group (n=9136)	SSR group (n=537)	*p* value
Sex, male	6220 (64.3)	5847 (64.0)	373 (69.5)	0.010
Age (yr)	50 (34–60)	50 (35–60)	57 (50–65)	<0.001
SBP (mm Hg) (n=8173)	130 (117–148)	132 (120–149)	88 (75–127)	
Mental status (n=8519)				
Alert	8372 (98.3)	8010 (100.0)	362 (71.1)	
Verbal	76 (0.9)	0 (0.0)	76 (14.9)	
Pain	23 (0.3)	0 (0.0)	23 (4.5)	
Unresponsive	48 (0.6)	0 (0.0)	48 (9.4)	
Sting to ED arrival time (min)	60 (30–248)	60 (30–276)	60 (33–121)	0.019
Season				<0.001
Spring	743 (7.7)	710 (7.8)	33 (6.2)	
Summer	4956 (51.2)	4657 (51.0)	299 (55.7)	
Autumn	3867 (40.0)	3677 (40.3)	190 (35.4)	
Winter	107 (1.1)	92 (1.0)	15 (2.8)	
Year of injury				0.259
2011	564 (5.8)	533 (5.8)	31 (5.8)	
2012	1106 (11.4)	1036 (11.3)	70 (13.0)	
2013	929 (9.6)	885 (9.7)	44 (8.2)	
2014	1509 (15.6)	1417 (15.5)	92 (17.1)	
2015	844 (8.7)	804 (8.8)	40 (7.5)	
2016	1937 (20.0)	1836 (20.1)	101 (18.8)	
2017	687 (7.1)	636 (6.9)	51 (9.5)	
2018	644 (6.7)	612 (6.7)	32 (6.0)	
2019	1453 (15.0)	1377 (15.1)	76 (14.2)	
Hospitalization	266 (2.8)	0 (0.0)	266 (49.5)	
Death	38 (0.4)	0 (0.0)	38 (7.1)	

SSR, severe systemic reaction; SBP, systolic blood pressure; ED, emergency department.
Data are presented as n (%) or median (inter-quartile range).

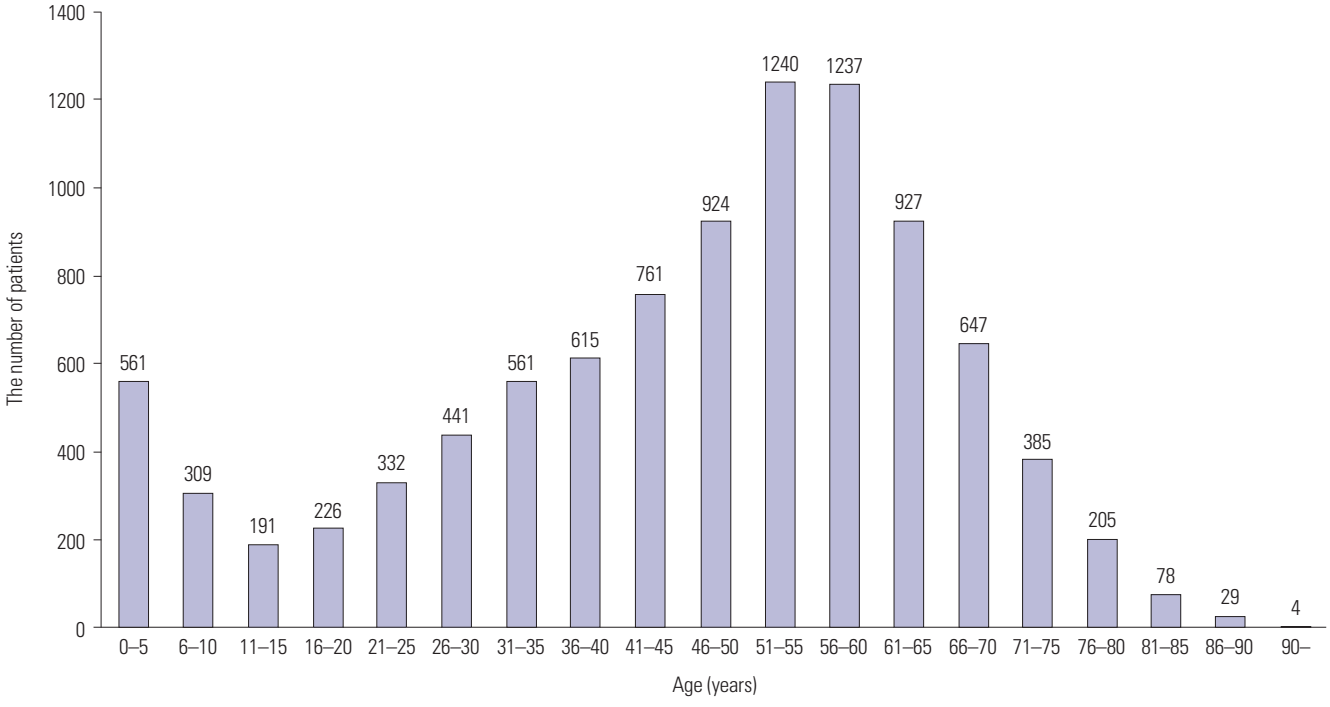

Fig. 1. Number of patients by age group divided into 5-year intervals.

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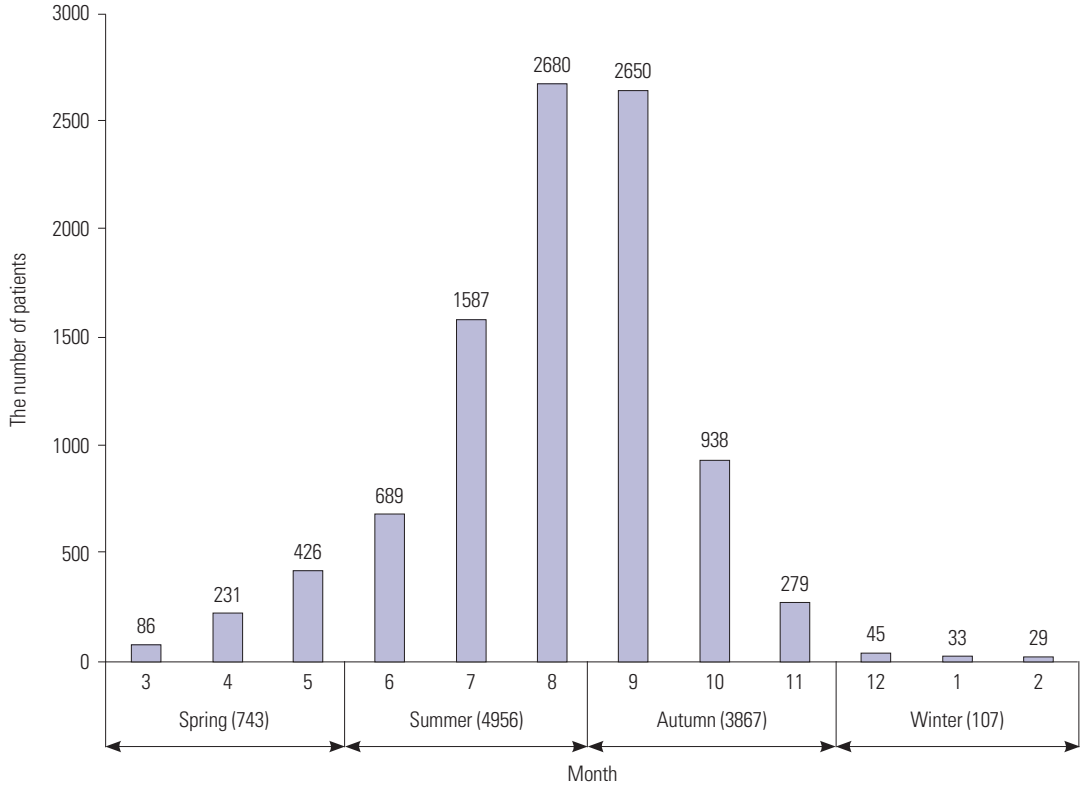

Fig. 2. Number of patients per month and season.

Table 2. Comparison of Injury Characteristics between the SSR and Non-SSR Groups

	Total (n=9673)	Non-SSR group (n=9136)	SSR group (n=537)	*p* value
Geographical location (n=9392)				<0.001
Residential area	1600 (17.0)	1531 (17.3)	69 (13.1)	
Public area	1152 (12.3)	1103 (12.4)	49 (9.3)	
Educational facilities	114 (1.2)	114 (1.3)	0 (0.0)	
Industrial/construction site	174 (1.9)	155 (1.8)	19 (3.6)	
Other outdoor places	6352 (67.6)	5962 (67.3)	390 (74.0)	
Type of activity at the time of sting (n=9502)				<0.001
Daily activities	5287 (54.7)	5000 (55.7)	287 (54.3)	
Occupational activities	1287 (13.3)	1174 (13.1)	113 (21.4)	
Education	88 (0.9)	87 (1.0)	1 (0.2)	
Leisure activities	2820 (29.2)	2695 (30.0)	125 (23.6)	
Others	20 (0.2)	17 (0.2)	3 (0.6)	
Anatomical site (n=4863)				0.003
Head and face	1017 (20.9)	963 (20.6)	54 (29.0)	
Neck	186 (3.8)	182 (3.9)	4 (2.2)	
Trunk	207 (4.3)	194 (4.2)	13 (7.0)	
Hand	1385 (28.5)	1350 (28.9)	35 (18.8)	
Arm	584 (12.0)	566 (12.1)	18 (9.7)	
Foot	337 (6.9)	326 (7.0)	11 (5.9)	
Leg	417 (8.6)	403 (8.6)	14 (7.5)	
2 or more sites	730 (15.0)	693 (14.8)	37 (19.9)	
Apitherapy (n=6031)	83 (1.4)	71 (1.3)	12 (3.1)	0.002

SSR, severe systemic reaction.
Data are presented as n (%).

Factors associated with SSRs

Table 3 presents the results of logistic regression analysis to identify risk factors contributing to the occurrence of SSRs. Male sex (OR 1.634, 95% CI 1.133–2.357) and increasing age (OR 1.030, 95% CI 1.020–1.041) were associated with the incidence of SSRs. Apitherapy (OR 3.685, 95% CI 1.408–9.641) and bee stings in the winter (OR 4.573, 95% CI 1.420–14.723) increased the risk of SSRs. The risk of SSRs was higher at industrial/construction sites (OR 2.691, 95% CI 1.012–7.154), compared to that of stings inflicted at residential areas, as well as for stings occurring during occupational activities (OR 1.897, 95% CI 1.228–2.932), compared to those occurring during daily activities. In cases of single-site stings, SSR risk was higher on the trunk and head/face than on the hands (OR 2.858, 95% CI 1.405–5.815 and OR 2.123, 95% CI 1.333–3.382, respectively). The time from sting to ED arrival was not associated with the risk of SSRs (p=0.019).

Mortality after bee sting injuries

A total of 38 deaths following bee stings were identified. Their characteristics are briefly presented in Table 4. Notably, most of these patients were male (65.8%), with a median age of 60 years (range: 46–78 years). More than half (52.6%) occurred in the summer, whereas none occurred during the winter when the risk of SSR is considered highest. Among the 18 patients whose sting site was identified, the highest incidence of fatality was observed after a sting localized in the head/face (61.1%), followed by that of stings occurring at two or multiple sites (16.6%). Only 17 cases had detailed information of the bee sting accident, which is summarized in Table 5. Most were stung outdoors, such as in rice fields or mountains. Eleven patients were stung in the head/face and seven suffered cardiac arrest before arriving at the hospital.

Table 3. Results of Univariable and Multivariable Logistic Regression Conducted to Detect Risk Factors for Bee Sting Associated Severe Systemic Reactions

Variables	Odds ratio (95% confidence interval)	
	Univariable analysis	Multivariable analysis
Sex, male	1.279 (1.060–1.545)	1.634 (1.133–2.357)
Age (yr)	1.035 (1.029–1.040)	1.030 (1.020–1.041)
Sting to ED arrival time (min)	1.000 (1.000–1.000)	
Apitherapy (n=6031)	2.541 (1.366–4.726)	3.685 (1.408–9.641)
Season		
Spring	Reference	Reference
Summer	1.381 (0.956–1.996)	1.039 (0.521–2.070)
Autumn	1.112 (0.762–1.623)	1.011 (0.499–2.050)
Winter	3.508 (1.835–6.705)	4.573 (1.420–14.723)
Geographical location (n=9392)		
Residential area	Reference	Reference
Public area	0.986 (0.678–1.433)	1.519 (0.759–3.041)
Industrial/construction site	2.720 (1.595–4.639)	2.691 (1.012–7.154)
Other outdoor places	1.451 (1.117–1.886)	1.553 (0.906–2.663)
Type of activity at the time of sting (n=9482)		
Daily activities	Reference	Reference
Occupational activities	1.677 (1.337–2.104)	1.897 (1.228–2.932)
Education	0.200 (0.028–1.443)	-
Leisure activities	0.808 (0.652–1.002)	0.889 (0.603–1.312)
Anatomical site (n=4863)		
Hand	Reference	Reference
Arm	1.227 (0.689–2.184)	1.020 (0.533–1.952)
Foot	1.301 (0.654–2.590)	1.342 (0.604–2.984)
Leg	1.340 (0.714–2.515)	1.350 (0.675–2.701)
Head and face	2.163 (1.402–3.336)	2.123 (1.333–3.382)
Neck	0.848 (0.298–2.413)	1.072 (0.368–3.123)
Trunk	2.585 (1.344–4.972)	2.858 (1.405–5.815)
2 or more sites	2.059 (1.286–3.299)	1.431 (0.864–2.368)

ED, emergency department.

Table 4. Summary of Demographic Characteristics and Nature of Injury for Patients Who Died from Bee Stings

Variables	Statistics
Sex, male	25 (65.8)
Age (yr)	60 (56–67)
Sting to ED arrival time (min)	76 (45–158)
Season	
Spring	1 (2.6)
Summer	20 (52.6)
Autumn	17 (44.7)
Winter	0
Geographical location (n=37)	
Residential area	0
Public area	2 (5.4)
Educational facilities	0
Industrial/construction site	0
Other outdoor places	35 (94.6)
Type of activity at the time of sting (n=35)	
Daily activities	12 (34.3)
Occupational activities	12 (34.3)
Education	0
Leisure activities	11 (28.9)
Others	0
Anatomical site (n=18)	
Head and face	11 (61.1)
Neck	1 (5.5)
Trunk	1 (5.5)
Hand	1 (5.5)
Arm	1 (5.5
Foot	0
Leg	0
2 or more sites	3 (16.6)

ED, emergency department.
Data are presented as n (%) or median (inter-quartile range).

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Table 5. Description of Accidents for Patients who Died from Bee Stings

Year	Season	Age/Sex	Sting site	Details of the bee sting injury
2012	Spring	73/M	Hand	The patient experienced a bee sting on the back of his right hand while walking down the street.
2012	Autumn	68/M	Head and face	The patients had hypersensitivity to bee venom. He was stung in the head by a bee while mowing grass in the mountains. He was in cardiac arrest when paramedics arrived.
2013	Autumn	58/M	Head and face	The patient developed dizziness and subsequently dyspnea after being stung on his nose. Despite alerting the EMS, the patient arrived at the ED in cardiac arrest.
2013	Autumn	49/M	Head and face	This patient was stung by bees in two places on the head and lips while mowing grass. He subsequently had dyspnea and called the EMS.
2013	Autumn	64/M	Head and face	The patient was stung thrice in the head by wasps in the mountains. He was transferred to the ED in cardiac arrest.
2014	Summer	73/M	Neck	The patient was stung in the back of the neck several times while cutting down a tree branch in the mountains. He subsequently vomited and developed cyanosis. He was in cardiac arrest when the paramedics arrived.
2014	Summer	72/F	Head and face	The patient collapsed after multiple stings on her face by wasps while working in the field. She was found by a passerby who alerted the EMS. She was transferred to the ED in cardiac arrest.
2014	Summer	64/M	Head and face	The patient was stung in the face by a bee while cleaning the front of a factory. Soon after, he vomited and lost consciousness. He was unconscious when the paramedics arrived, and ventricular fibrillation was observed during transport.
2014	Autumn	46/M	Head and face	The patient was found collapsed while working in a rice field. A beehive was spotted next to the patient and several bees were attached near his ears.
2014	Autumn	65/M	Arm	The patient was likely stung once by a wasp on the back of his right arm while working at a plastic greenhouse.
2016	Summer	52/M	Head and face	The patient was stung in his right eye by a bee. Subsequently, he developed swelling and foreign body sensation in the eye.
2016	Summer	69/F	Head and face	The patient was stung on the vertex of her head by a bee. She eventually felt dizzy and lost consciousness in the bathroom.
2016	Autumn	58/M	Unknown	The patient called his family complaining about a bee sting in the mountains. Paramedics found the patient in cardiac arrest.
2017	Summer	60/F	Head and face	The patient was stung in the head by a bee while working on her farm.
2018	Summer	57/M	Unknown	The patient was presumably stung by a bee while working in the field and eventually lost consciousness.
2018	Summer	60/F	Head and face	The patient was stung in the head by a bee while working on a farm.
2019	Autumn	78/F	2 or more sites	After being stung by a bee all over her body the patient visited a local hospital. Her troponin I levels increased to 0.11, and she was transferred to another hospital.

ED, emergency department; EMS, emergency medical service.

DISCUSSION

In this study, the composite outcome variable SSR was used, which was defined as having one of the following: hypotension, altered mental status, hospitalization, or death. In previous studies, the diagnosis of anaphylaxis or death was usually used as an outcome variable and indicator of SSRs. However, caution must be exercised when using research methodology based on anaphylaxis codes entered at the ED. Previous ED-based studies have indicated that diagnosis of anaphylaxis in the ED is inconsistent.[11-13] Consequently, because this study was based on data collected in the ED, the diagnosis of anaphylaxis was not considered reliable.

The number of patients under 15 years of age with bee stings tended to decrease with increasing age, which was consistent with other studies.[5,14] The reason for the higher frequency of bee stings in younger children is that bees are portrayed as "friendly" in images and videos to which children are exposed; therefore, children may approach them without recognizing their potential danger. Furthermore, children often walk barefoot on grass where bees frequently forage.[5,14] Compared with adults, children may be more easily attacked because they lack the ability to avoid dangerous situations, such as recognizing a beehive, chasing bees, or running away when attacked. However, these results might be biased, owing to differences between the total number of patients with bee stings and those who visit the hospital. Parents of younger children tend to seek medical attention even for mild local reactions, whereas older children and adults do not.[5]

In this study, the proportion of affected males was higher than that of females. These results were similar to previously reported values (60%–64%).[5,15] Kono, et al.[5] explained that males are more likely to be stung by bees because they are more engaged in beekeeping. In this study, the patients who were stung during daily (non-occupational) activities were mostly male (62.1%). Therefore, the differences between sexes could not be adequately explained solely based on occupation. Notman and Beggs[16] reported that males tended to be less careful when

handling bees than females, which might also increase bee sting-related injuries. Therefore, considering that the proportion of male patients with bee stings is high even in non-occupational activities measured in this study, we believe that the latter interpretation is likely more relevant. Males also had a higher risk of SSRs from bee stings. Previous reports from various countries have also indicated a high proportion of men among severely ill patients who were hospitalized or died owing to bee sting injuries.[17-19] This may be a direct consequence of the increased propensity of being stung more than females. However, males might also have a higher rate of hypersensitivity to bee venom than females.[20] This high rate of hypersensitivity to bee venom may be one of the contributing risk factors for developing an SSR.

Late summer was consistently considered as the season with the highest occurrence of bee stings. This is because the breeding season of bees starts in spring, and their population size reaches a maximum in late summer.[5,21] Additionally, the increased occurrence of bee stings may be attributed to shorter clothing and more skin exposure in summers. Beekeepers know empirically that bees are more dangerous in the winter.[22] Woyke[23] reported that bees are more aggressive in winters than that in summers, but they could not confirm whether more severe reactions occurred in patients who were stung by bees in the winter.[23] This study showed that when bee stings occurred in the winter, the risk of an SSR was approximately 4.6 times higher than those in the spring. As the flying activities of bees and outdoor activities of humans decrease during winter, bee stings likely occur when the beehive exists within the activity zone of the patient. This condition would increase the possibility that patients stung during the winter would be naturally exposed to bee venom in their daily lives. This may have caused the patient to develop hypersensitivity to bee venom. Disturbing beehives in the winter is dangerous because the more aggressive bees are densely nested instead of foraging; thus, bee sting accidents near the hive in the winter might increase the probability of being attacked by several bees. The composition of bee venom varies with seasons.[24] However, we lack studies on whether these differences in composition have varied effects on the human body.

In this study, the most frequent single-sting sites on the body included the hands, head/face, and arms, which is consistent with previous findings.[19,25] Traditionally, the risk of anaphylaxis increases with stings on the head or neck.[8] However, recent studies that reported that bee stings on the head and neck do not increase the risk of anaphylaxis.[26,27] This study revealed that a sting on the head/face and torso is more likely to cause a severe reaction than stings elsewhere. The head includes the entry points of the upper airways, such as the nose and mouth; stings in these areas result in local reactions, such as obstruction of the upper airway without an anaphylactic reaction, which may require hospitalization. Therefore, the different results may be attributed to anatomical characteristics of the head and differences in outcome variables. The trunk has the largest surface area among the body parts considered in this study. Therefore, multiple stings are more likely to occur on the trunk, thereby resulting in a higher risk of an SSR in patients with trunk stings than in those with stings on other body parts.

SSRs were more likely to occur in bee sting injuries during occupational activities and industrial/construction sites. Industrial/construction site workers, however, are highly unlikely to visit the ED during working hours on account of a mild local reaction from a bee sting. Therefore, this result may be biased because only patients with relatively severe symptoms visited the ED.

In this study, SSRs occurred in 12 of 83 patients who received apitherapy (bee venom acupuncture), which has been identified as an independent risk factor for the occurrence of SSRs. Lee, et al.[28] recently reported that anaphylaxis occurred in 15 of 8580 patients (0.2%) who received apitherapy. Their study only targeted patients who received apitherapy by licensed professionals. However, in this study, approximately 1/3 of the cases revealed that apitherapy was performed by neighbors or the patients themselves. Among them, two patients used live bees to sting their bodies. Although, apitherapy uses pure melittin products extracted from bee venom to reduce allergic reactions,[29] the possibility of using unauthorized products in unlicensed procedures cannot be ruled out.

A statistical correlation was not observed between the year of the bee sting and SSR incidence; however, there was a large difference in the number of patients with reported bee stings by year. In future studies, identifying the cause of such differences could help predict the risk period of bee sting accidents and contribute to preventing them.

The present study has several limitations. First, this study included only data collected in one country; therefore, the results cannot be generalized to other countries because there may be differences in the species of inhabitant bees or accessibility to EDs. Second, the criteria for identifying severe reactions in this study differ from those of previous studies investigating bee sting injuries. Therefore, caution must be exercised when comparing these results with those of previous studies. Third, a bee sting, the major inclusion criteria, was based on statements from the patients. Some patients may have confused a sting or bite from another insect with that of a bee sting. Furthermore, several patients could not distinguish between hornets and honeybees. Although the effects of the venom of these two groups on the human body may differ, this information was not included in the data. Fourth, the higher the number of bee stings, the greater the possibility of a serious reaction. However, the number of stings was not collected in this study and, therefore, could not be included in the analysis. Fifth, owing to limitations of the multicenter registry data that were retrospectively collected, detailed medical information for each patient could not be obtained. Previous experience of exposure to bee venom and a history of cardiovascular disease, which are well-known risk

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factors for systemic reactions to bee venom, were not recorded. Moreover, we could not assess the reason for hospitalization of each patient. For example, acute kidney injury and/or rhabdomyolysis could be one of the reasons for hospitalization. Additionally, anaphylaxis and systemic toxicity, which have different mechanisms and risk factors, could not be distinguished. Therefore, further studies based on data containing this detailed medical information should be conducted.

In summary, bee sting injuries require further attention as they occasionally lead to SSRs, including fatality. The frequency of bee sting accidents is high among young children who do not recognize the danger of bees and have a low self-protection ability; therefore, safety measures should be developed to avoid injuries for this age group. Safety education for infants and young children, who are often stung by bees, and the older population, who are at high risk of an SSR, should be implemented. Despite the rarity of bee stings in the winter, caution must be exercised as the risk of an SSR is 4.6 times higher than that in spring. Finally, a robust policy to reduce unauthorized apitherapy practiced by laypeople is required.

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AUTHOR CONTRIBUTIONS

Conceptualization: Ji Hwan Lee and Sung Phil Chung. Data curation: Ji Hwan Lee and EungNam Kim. Formal analysis: Ji Hwan Lee and Sung Phil Chung. Funding acquisition: Min Joung Kim. Investigation: Min Joung Kim. Methodology: Ji Hwan Lee and Sung Phil Chung. Project administration: Sung Phil Chung. Resources: Min Joung Kim and EungNam Kim. Software: Ji Hwan Lee. Supervision: Yoo Seok Park and Hyun Soo Chung. Validation: Ji Hwan Lee. Visualization: Ji Hwan Lee. Writing—original draft: Ji Hwan Lee. Writing—review & editing: Sung Phil Chung. Approval of final manuscript: all authors.

ORCID iDs

Ji Hwan Lee https://orcid.org/0000-0002-6908-9459
Min Joung Kim https://orcid.org/0000-0003-1634-5209
Yoo Seok Park https://orcid.org/0000-0003-1543-4664
EungNam Kim https://orcid.org/0000-0003-3221-2254
Hyun Soo Chung https://orcid.org/0000-0001-6110-1495
Sung Phil Chung https://orcid.org/0000-0002-3074-011X

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