

# Population-Based Study of the Epidemiology of Herpes Zoster in Korea

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General epidemiological data regarding herpes zoster (HZ) are necessary for treatment and prevention of this disease. In addition, epidemiological data can play an important role in evaluating the efficacy and impact of vaccination. Though several epidemiological studies of HZ in Korea have been conducted, they usually depend on hospital-based data and may not be representative of HZ characteristics all over Korea. The purpose of this study was to evaluate the incidence and other epidemiological features of HZ in the general Korean population. We used population-based medical records from the Health Insurance Review & Assessment Service, which includes 50,908,646 medical insurance subscribers, to calculate the incidence of HZ. Also, we analyzed an age-stratified random sample of 1,375,842 individuals to study descriptive epidemiologic characteristics of HZ in Korea in 2011. We observed that the incidence of HZ was 10.4 per 1,000 person-years and was strongly correlated with age. Sex had a major influence on HZ incidence; overall, there were 12.6 cases per 1,000 person years in women and 8.3 cases per 1,000 person years in men. There was no difference in incidence according to the locality and season.

**Keywords:** Herpes zoster; Epidemiology; Population-Based Study; Korea

## INTRODUCTION

Herpes zoster (shingles, HZ) is caused by reactivation of the varicella-zoster virus (VZV). This virus can remain latent in neurons of cranial nerve ganglia, dorsal root ganglia, and autonomic ganglia along the entire neuroaxis after primary infection with varicella (chickenpox), which usually occurs in childhood. It is characterized by a maculopapular or vesiculobullous rash along skin dermatomes, with severe pain (1).

The most common complication of HZ is postherpetic neuralgia (PHN), or persistent pain lasting more than 3 months after the skin rash, even though the precise definition of PHN has not been defined yet. PHN can negatively affect quality of life, including physical, emotional, and social functioning, and may interfere with quality of life to a degree similar to congestive heart failure, depression, acute myocardial infarction, and diabetes (2).

The live attenuated vaccine against HZ (Zostavax<sup>®</sup>) was recently introduced worldwide, and is recommended for people aged 50 yr or above with no contraindications. The efficacy of the vaccine in people over 60 yr old is 53% for the prevention of HZ and 65% for the prevention of PHN lasting 90 days or more (3). For people aged 50-59 yr old, the efficacy for HZ prevention is 70% (4). Despite the lack of population-based data, including the epidemiology of HZ in Korea, Zostavax<sup>®</sup> was approved in

2009 by the Ministry of Food and Drug Safety of Korea.

General epidemiological data of HZ are necessary for the treatment and prevention of this disease. In addition, they can help to evaluate the efficacy and impact of vaccination. Though several epidemiological studies of HZ in Korea have been conducted, they usually depend on hospital-based data and may not be representative of HZ characteristics all over Korea (5-7). The purpose of this study was to evaluate the incidence and other epidemiological features of HZ in the general Korean population.

## MATERIALS AND METHODS

### Data source and case definition

In Korea, almost all citizens have been covered by the National Health Insurance Service (NHIS) since 1989. All demographic data including age and sex are collected under the NHIS according to the patient's Korean ID number. Because the Health Insurance Review & Assessment Service (HIRA) was developed for medical billing purposes at the NHIS, all medical acts including diagnosis, physical and laboratory examination, treatment, prescription, nursing acts, and hospitalization are recorded relatively precisely in a computerized database along with the individual's Korean ID number. Thus, the deduction of incidence was based on data that covered 50,908,646 medical in-

surance subscribers in 2011. Descriptive epidemiological data were drawn from age-stratified random sample records of the patients. These included the medical records of 3% of all patients who used the medical service, covering 1,375,842 individuals during the period of January 1, 2011 through December 31, 2011 (8). The residence distribution of the population used in the study was derived from the national residence registration data from 2011.

HZ cases were identified through a database search for any subject with the HZ-related International Classification of Disease 9th revision code (ICD-9 code, 053) except PHN, and the relevant domestic HIRA code for HZ (B02). As we investigated incidence during a relatively short period of time, we could not consider recurrent cases in this study.

**Statistics**

All outputs were produced using SPSS, version 20.0 (IBM SPSS, Inc. in Chicago, IL, USA) for statistical analysis. All variables were described by number or percentage.

**Ethical considerations**

The study protocol abided by the principles of the Declaration of Helsinki and was approved by the institutional review board (IRB) of Seoul St. Mary’s Hospital (IRB No. KC14RIMI0137). Informed consent was waived by the IRB.

**RESULTS**

**HZ incidence**

During the study period, 529,690 individuals with HZ were identified, corresponding to the incidence of 10.4 per 1,000 person-years in all age groups. The incidence of the disease was strongly correlated with age, and more than half of the patients were over 50 yr old. The age-adjusted incidence increased with age, ranging from 2.0 per 1,000 person-years in the childhood group to 21.8 per 1,000 person-years in 70-79 yr-old patients. A striking increase in HZ incidence was seen over the age of 50 yr. Peak HZ incidence was observed in patients aged 60-69 yr, with 22.4

per 1,000 person-years. In patients over 80 yr old, the incidence was reduced to 16.5 per 1000 person-years (Table 1).

Out of 529,690 patients, 211,635 (40.0%) were men and 318,055 (60.0%) were women, with a relative ratio of 0.67. The incidence rate was also higher in women than in men, with 12.6 per 1,000 person-years in women vs 8.3 per 1,000 person-years in men. Based on age-specific incidence data, this trend was observed in all age groups (Fig. 1).

**Regional distribution of HZ cases**

We used an age-stratified random sample of 18,719 HZ patients to gather more detailed descriptive epidemiology statistics. Fig. 2 shows the number of HZ cases by province and the relative incidence of HZ, taking the population density of each province into consideration. There was no significant difference in relative incidence between provinces.

**Seasonal variation of HZ cases**

We used an age-stratified random sample for the seasonal variation of HZ. The occurrence of HZ cases was not significantly

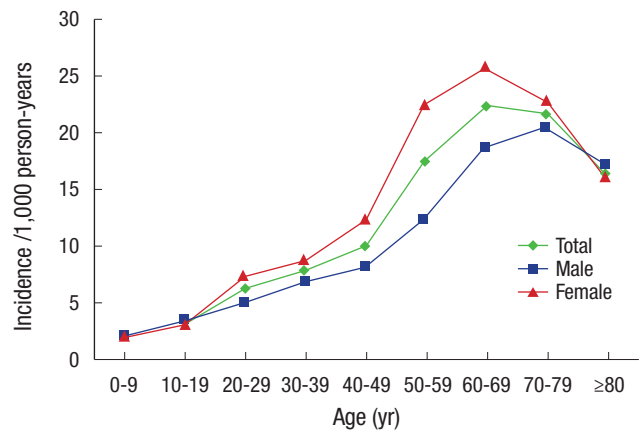


Fig. 1. Age-adjusted incidence of herpes zoster according to sex.

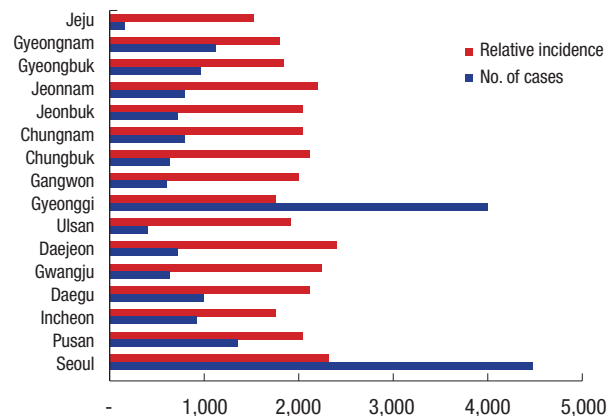


Fig. 2. Number of cases and relative incidence of herpes zoster by province. Relative incidence was calculated based on the national population and house census undertaken in 2011.

Table 1. Age adjusted incidence of herpes zoster per 1,000 person-years in Korea

Age group (yr)	No. of cases	% of cases	Population	Incidence /1,000 person-years
0-9	9,500	1.8	4,675,849	2.0
10-19	22,362	4.2	6,681,125	3.3
20-29	42,191	8.0	6,727,416	6.3
30-39	64,693	12.2	8,254,786	7.8
40-49	90,347	17.1	8,846,683	10.2
50-59	130,924	24.7	7,528,146	17.4
60-69	94,439	17.8	4,216,872	22.4
70-79	60,286	11.4	2,771,176	21.8
≥ 80	16,994	3.2	1,032,231	16.5
Total	529,690	100	50,734,284	10.4

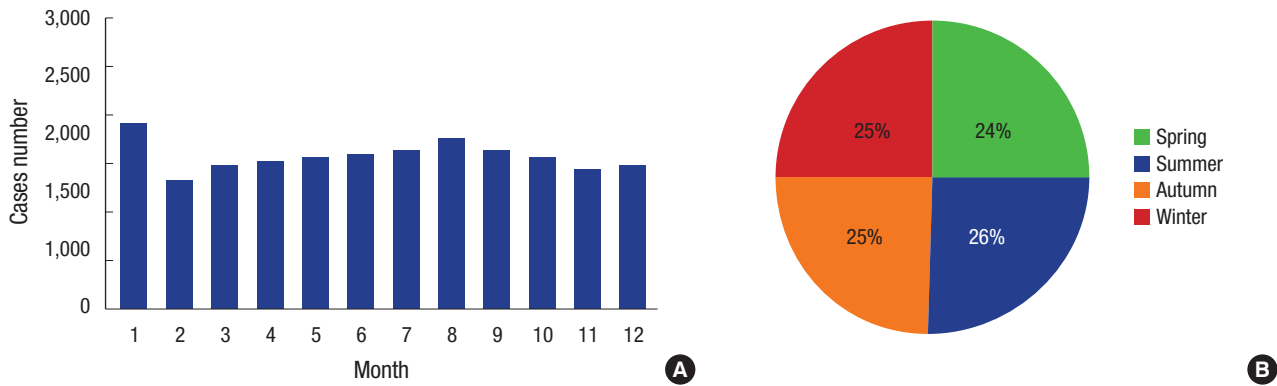


Fig. 3. Number of patients herpes zoster. (A) Monthly occurrence. (B) Seasonal occurrence.

Table 2. Characteristics of hospitalization in herpes zoster patients

Age group (yr)	No. of cases	% of cases	No. of HZ	Hospitalization rate
0-9	5	0.5	356	14.0
10-19	26	2.8	827	31.4
20-29	35	3.8	1,473	23.8
30-39	68	7.4	2,120	32.1
40-49	114	12.4	3,170	36.0
50-59	219	23.9	4,700	46.6
60-69	172	18.8	3,235	53.2
70-79	169	18.4	2,164	78.1
≥ 80	109	11.9	674	161.7
All	917	100.0	18,719	49.0

different from month to month in 2011; January 1,906, February 1,313, March 1,464, April 1,489, May 1,549, June 1,567, July 1,628, August 1,747, September 1,624, October 1,526, November 1,440, and December 1,466 cases (Fig. 3A). Categorizing the cases according to the season of occurrence, each of spring (March, April, and May), summer (June, July, and August), autumn (September, October, and November), and winter (December, January, and February) comprised 24.1%, 26.4%, 24.5%, 25.0% of the cases, respectively (Fig. 3B). There is no seasonal variation of HZ cases.

#### Hospitalization and usage of medical institution

A total of 917 HZ patients were hospitalized during the study period. The hospitalization rate (number of patients hospitalized per 1,000 cases of HZ) was inversely correlated with age, ranging from 14.0 per 1,000 cases of HZ in childhood to 161.7 per 1,000 cases of HZ in age group over 80 (Table 2).

In Korea, there are several grades of medical institutions, including primary health care facilities, semi-hospitals, and general hospitals. Primary health care facilities are usually out-patient based clinics, and both semi-hospitals and general hospitals are held to higher standards by the law and are capable of treating patients with more severe illnesses. Fig. 4 shows that a larger proportion of elderly patients used hospitals, when compared to younger patients.

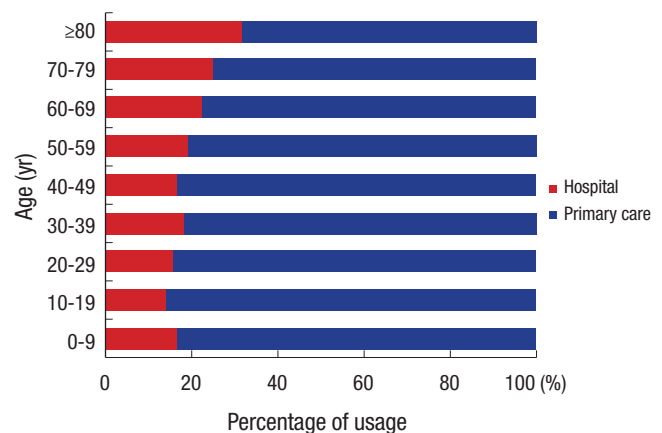


Fig. 4. Usage of medical institutions according to the age.

## DISCUSSION

We found that the incidence of HZ is 10.4 per 1,000 person-years, and is strongly correlated with age. The calculated incidence in this study is much higher than that of previous studies conducted on different populations in the United States, Canada, South America, Europe, Asia, and Australia; these studies revealed a median HZ incidence of 4-4.5 per 1,000 person-years (9). These differences are highly dependent on the methodology used, the definition of the disease, and demographic features of the sample population.

This relatively higher incidence can be explained in part by the recent understanding of the medical service system and social attention to HZ in Korea. All Korean citizens have been obligatorily covered by NHIS since 1989, with relatively lower medical costs. For example, the mean medical cost paid by the patients for medical consultation, prescription, and other medical treatment, including hospitalization for HZ, was less than 45,000 KRW (approximately 42 USD) in 2011 (10). This insurance system facilitated the use of the medical service. Consequently, 89.1% of the covered persons used the medical service more than once, with a mean of 18.4 days visiting the system in 2011

(11). Therefore, it is likely that our data covers a relatively large number of cases with mild symptoms and low socioeconomic status. In addition, HZ with a characteristic skin rash is one of the best known skin diseases in Korea and is notorious for terrible pain. Therefore, people with suspected symptoms tend to visit the hospital for diagnosis and treatment. These environmental situations can influence the incidence of HZ found in this study.

Another explanation for the higher incidence is that this study was based on relatively recent data. In previous studies with an extended time period, the age-adjusted incidence of HZ is increasing. For example, in Olmsted County of the United States, HZ rates increased 28% over 5 yr, from 3.2 per 1,000 person-years in 1996-1997 to 4.1 in 2000-2001 (12). The incidence in Taiwan jumped by 54.8%, from 4.82 per 1,000 person-years in 2000 to 6.89 per 1,000 person-years in 2008 (13). Although the reason for the increase remains unclear, it seems to be related to an increase in the elderly population and in the prevalence and treatment of chronic diseases that weaken the immune system.

Based on our results, sex is the most important factor that determines HZ incidence. In most age groups, the female HZ incidence was higher than the male HZ incidence, with 12.6 per 1,000 person-years in women and 8.3 per 1,000 person-years in men overall. Thus, the incidence of HZ is 1.5 times higher in women. Previous studies also reported a higher incidence of HZ in women, with a relative risk in the range of 1.2-1.47 (14-16). This is due to the natural characteristics of HZ as well as the fact that women use more medical services than men within the elderly Korean population. According to the data from the Korean Statistical Service, the rate of the medical service use per person in men over 50 yr old was 25.1 per years and 33.8 per years in women in 2011 (11).

Age is another important factor that determines the incidence of HZ. This is attributable to the progressive decline in cell mediated immunity (CMI) to VZV. T-CMI is more important than antibodies for preventing VZV reactivation. VZV-specific T-CMI declines with age, even during the first 3 yr after varicella, which is accompanied by a decrease in VZV-specific memory CD4 T cells (9).

In this study, the incidence rate of HZ was not varied by province. The lack of differences between provinces reflects the homogeneous ethnic group and the relatively constant climate in Korea. We also observed that there was no seasonal difference in the incidence of HZ. These results support previous reports concluding that there is no seasonal variation in the incidence of HZ (5-7).

This study is limited by its reliance on the computerized database instead of the medical records including symptoms and signs; because of this, cases that were misdiagnosed or over-diagnosed could not be eliminated. In spite of these limitations, however, the present study is the first population-based descrip-

tive epidemiological study of HZ in Korea that includes incidence categorized by age, sex, and other characteristics of HZ.

## DISCLOSURE

The authors have no conflict of interest to declare.

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