Background and Objectives The seasonality and climatic relevance of epiglottitis have not yet been fully investigated in a population-based cohort. This study aimed to examine the seasonality of epiglottitis and explore associated climatic factors.

Materials and Method In a retrospective cohort study using the Korean National Health Insurance claims database from January 2010 to December 2019, we identified patients with epiglottitis who claimed the following diagnostic codes as a principal or first additional diagnosis: International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes J0510, J0510.001 (acute epiglottitis without obstruction, epiglottitis not otherwise specified), and J0511 (acute epiglottitis with obstruction). We calculated the seasonal ratio as the ratio of the highest to the lowest number of patients per month to compare the degree of seasonality. In addition, the climate data points corresponding to each month were obtained. Thus, we analyzed the correlations between the monthly patient numbers for each disease and various climatic factors.

Results There were seasonal variations in the number of patients with epiglottitis, which were highest from winter to spring and lowest in summer. The prevalence of epiglottitis was strongly correlated with the average temperature, ground temperature, relative humidity, precipitation, daily temperature range, and sunlight rate. Additionally, epiglottitis was most prevalent in the <9 age group before 2013, but after 2013, it was most prevalent in the 30–39 age group.

Conclusion This large population-based study demonstrated clear seasonality and climatic association in patients with epiglottitis. Further studies exploring the detailed demographic factors affecting epiglottitis are required to address similar diseases more effectively.

Keywords Epiglottitis; Seasonality; Epidemiology.

INTRODUCTION

Acute epiglottitis refers to inflammation in the epiglottis and the adjacent laryngeal structures. It can be life-threatening and lead to fatal upper airway obstruction in a matter of hours, even in previously healthy patients. In the past, this disease was commonly observed in children and was primarily caused by Hemophilus influenza type b (Hib) [1]. The
Acute epiglottitis is considered an upper respiratory tract infection. Climate and humidity are strongly associated with upper respiratory tract infections, as exposure to cold temperatures and dry air can lower the body temperature and cause cold stress, which weakens the immune system, making it more susceptible to infection [6,7]. Acute epiglottitis is also an infectious disease that occurs in the upper respiratory tract, and there may be a link between climate change and its prevalence. However, to date, there have been few studies on the link between epiglottitis and climate change, particularly those investigating different correlations between epiglottitis and season [8-10].

Thus, we aimed to analyze the correlation between climate and the prevalence of epiglottitis based on large-scale data from a population-based cohort reflecting the entire population of one country. In this study, we overcame many of the technical shortcomings of previous studies and obtained more accurate information on the association between epiglottitis and climate. This will allow us to better understand acute epiglottitis and use the results for its prevention and treatment.

MATERIALS AND METHOD

Study population
This nationwide, population-based, cross-sectional study used compulsory health insurance claims data from the Korean National Health Insurance (NHI) database between January 2010 and December 2019. The Korean NHI claims database includes date of birth, region of residence, sex, and date of hospital visit.

We identified every patient with epiglottitis who claimed the following diagnostic codes as a principal or first additional diagnosis: International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes J05.1, J05.10 (acute epiglottitis, acute epiglottitis without obstruction, epiglottitis not otherwise specified), and J0511 (acute epiglottitis with obstruction). Patients were categorized according to the following age ranges: <9, 10–19, 20–29, 30–39, 40–49, 50–59, 60–69, and >70 years.

We calculated the seasonal ratio as the ratio of the highest to the lowest number of patients per month to compare the degree of seasonality [11]. However, each month may have a different number of working days due to vacations or national holidays. Thus, we standardized the monthly patient number of each disease with the patient number of diabetes mellitus (E10–15 and R81) under the assumption that diabetes mellitus would have the least seasonal variation.

This study was reviewed and approved by the Institutional Review Board (2022-05-060).

Correlation analysis between climate factors and epiglottitis
We acquired climatic data from the Korean Meteorological Administration for the aforementioned period. Climate data included average temperature, daily temperature range, relative humidity, monthly aggregate precipitation, sunlight rate, average ground temperature, particulate matter <10 μm (PM10), ultraviolet A dose, and ultraviolet B dose every month.

Pearson’s correlation was used to determine the correlation between the monthly patient numbers and various climatic factors associated with “epiglottitis.” Pearson’s correlation coefficients, including R and p-values, were calculated to determine the relevant climatic factors in epiglottitis.

Statistical analysis
The R software package (version 4.2.1; http://www.r-project.org) was used for all the statistical analyses. The prevalence of patients between 2010 and 2019 was visualized using the ggplot2 and ggpmisc packages. The annual incidence of each disease according to age and sex was also described. Correlations, including R and p-values, between monthly patient numbers and climatic factors were described using the ggpubr package. Statistical significance was set at p<0.05.

RESULTS

Tables 1 and 2 show the total number of patients in each year, the number of male and female patients, and the number of patients in each age group, respectively. Fig. 1 shows the seasonality of epiglottitis from 2010 to 2019. The number of patients diagnosed with epiglottitis was highest between December and April and lowest between June and August every year. In other words, patient numbers remained relatively high from winter to spring and were lowest in summer. The seasonal variation was
close to 2 for epiglottitis (seasonal ratio: 1.840) (Table 3).

In assessing prevalence by sex, female had a higher prevalence than male in every month of the study. In terms of age, prior to 2013, the highest prevalence was in the <9 age group, followed by the 30–39 and 40–49 age groups; however, after 2013, the prevalence in the <9 age group declined sharply, with the highest prevalence in the 30–39 age group. In contrast, those aged >70 years had the lowest prevalence across the study period (Fig. 2).

Additionally, we measured seasonality ratios according to age and sex (Table 3). The highest seasonality was observed in age group 10–19 (seasonal ratio: 2.688), followed by the 40–49 group (seasonal ratio: 2.183). The lowest seasonality (seasonal ratio: 1.858) was observed in the <9 age group. Seasonality was higher for females (seasonal ratio: 1.952) than for males (seasonal ratio: 1.725).

Analysis of Pearson’s R and p values indicated a negative correlation between epiglottitis and average temperature (0.294, p<0.05), average ground temperature (0.280, p<0.05), relative humidity (0.427, p<0.05), and monthly aggregate precipitation (0.257, p<0.05).
p<0.05) (Fig. 3A-D). However, the daily temperature range (0.325, p<0.05) and sunlight rate (0.246, p<0.05) were positively correlated with epiglottitis (Fig. 3E and F). There was no significant correlation between monthly particulate matter concentration (0.031, p<0.05) and average daily UV radiation (0.157, p<0.05) (Fig. 3G and H).

**DISCUSSION**

The present study analyzed the seasonality of epiglottitis according to patient sex and age. Between 2010 and 2019, the number of patients with epiglottitis was the highest from winter to spring and lowest in summer. Additionally, a female predomi-
nance has been observed. Patients aged <9 years were the most prevalent in epiglottitis before 2013, while 30–39 year old patients were the most prevalent after 2013.

Acute epiglottitis is an acute upper respiratory tract disease that occurs within a short period of time and causes pharyngeal pain, dysphagia, and progressive dyspnea. The disease is known to occur in all age groups, is more prevalent in males, and occurs predominantly in winter months, although there is no significant seasonal variation [12]. However, recent studies have shown conflicting results. One study reported no seasonal variations in the incidence of epiglottitis [8], while another revealed that hospitalizations due to epiglottitis were highest in December and lowest in April [9], and a third study reported them to be highest in summer [10]. This shows that the seasonal correlation of epiglottitis is not clearly established. However, these studies are limited by their small sample size [8], one-year inpatient data [10], or biennial inpatient data [9]. In contrast, our study analyzed 10 years of accumulated large-scale data using health insurance information, which is more suitable for seasonal correlation analyses.

Notably, the prevalence of epiglottitis in the patient age group <9 years was highest until approximately 2013, after which it decreased. This may be due to the fact that the Hib vaccine has been nationally administered since 2013 [13]. Hib vaccination has a substantial impact on reducing the incidence of acute epiglottitis in the pediatric age group and a relatively small impact in those 15 years and older [8,14]. The decrease in the incidence of epiglottitis in the under 10 age group since 2013 may reflect this.

In this study, we assessed climate data and corresponding patient data in one country, spanning a 10-year period and revealed that epiglottitis was negatively correlated with several climatic factors, including average temperature, ground temperature, relative humidity, and precipitation. In contrast, daily temperature range and sunlight rate were positively correlated with epiglottitis.

The reason for this predisposition can be assessed similar to that of an upper respiratory tract infection. Several studies have been conducted on the relationship between climate and humidity and the tendency to develop upper respiratory tract infections. The prevalence of upper respiratory tract infections increases in cold weather and at low relative humidity [6,7]. There are several possible explanations for this trend. First, cold weather can increase the frequency of exposure to bacteria and viruses that can cause upper respiratory tract infections, as many people live in close quarters indoors in unventilated environments, which can lead to an increase in incidence [15]. Second, the rapid drop in body temperature caused by cold temperature can cause vasoconstriction in the nasal cavity and upper respiratory tract, which can interfere with the upper respiratory tract's immune system and increase the likelihood of infection [16]. In addition, inhalation of cold, dry air can cause damage to the upper respiratory tract mucosa, making it more susceptible to infection [17]. Lastly, cold weather can inhibit ciliary movements in the mucous membranes, which can increase the prevalence of infection [18]. We can explain why the prevalence of epiglottitis is also negatively correlated with average temperature, ground temperature, and relative humidity, while being positively correlated with daily temperature range, for the reasons above. Precipitation is thought to be negatively correlated with the prevalence of epiglottitis, because more precipitation leads to higher relative humidity, whereas a higher sunlight rate is thought to be positively correlated with the prevalence of epiglottitis, because a higher sunlight rate leads to fewer cloudy days, creating an environment with lower relative humidity.

As an upper respiratory tract infection, acute epiglottitis may be expected to show a pattern of association with climate similar to that of other upper respiratory tract infections. However, few studies have been conducted reporting a variety of trends. The present study was a large-scale statistical analysis of 10 years of data. Therefore, the reliability of the results on the seasonal correlation of epiglottitis should be higher than that of previous studies. This direct link between acute epiglottitis and the climate may contribute to research on its prevention and treatment, which has been relatively neglected because of its low prevalence.

Our study has several limitations. First, the medical claims database uses diagnostic coding rather than medical chart records. Second, there is a lack of information on other social factors, such as medical history, smoking, and alcohol history, which may impact these diseases. However, these medical claims databases included most patients in South Korea, reducing selection bias as completely as feasible. Another limitation is that the analysis was not conducted for each diagnosis code group. For incidence, J0511 (acute epiglottitis with obstruction) is a code that can only be diagnosed when the symptoms are more severe than other diagnosis codes. However, this code was analyzed together with other less severe diagnosis codes. Further research should be conducted by analyzing diagnosis codes first and then assessing the severity of symptoms and their association with climate change. Finally, the unique characteristics of each region could not be considered because the monthly climate data used were the national average data of Korea. If further studies are conducted to analyze the incidence of acute epiglottitis in relation to climate characteristics in different cities, it will help in conducting more developed analysis of the association between acute epiglottitis and climate in Korea.

To the best of our knowledge, this is the first study to comprehensively analyze the seasonality and climatic relevance of epiglottitis using a large population database and meteorologi-
cal data. We focused not only on determining the seasonality of epiglottitis, but also on determining its correlation with detailed climate data during 10 years.

In conclusion, using a large population-based study, we confirmed the seasonal and climatic relevance of epiglottitis in patients between 2010 and 2019. Further studies exploring the detailed demographic factors affecting epiglottitis are required to address similar diseases more effectively.

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Conflicts of Interest
The authors have no financial conflicts of interest.

Authors’ Contribution
Conceptualization: Hun Hee Lee, Young Chan Lee, Young-Gyu Eun. Data curation: all authors. Formal analysis: Jong Hwan Lee, Su Il Kim, Young Chan Lee. Project administration: Young Chan Lee. Writing—original draft: Jong Hwan Lee, Su Il Kim. Writing—review & editing: all authors. Approval of final manuscript: all authors.

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