Background. An increase in the incidence of herpes zoster (HZ) is observed in South Korea. However, the effects of changes in population structure and immune status on the incidence and severity of HZ have not been well understood. We investigated longitudinal changes in the incidence of HZ and disease severity over time and according to age and comorbidities.

Methods. We used population-based medical records from the National Health Insurance Service for approximately 55,000,000 subscribers from 2000-2015. Herpes zoster cases (period 2003-2015) or its complications (period 2007-2015) were identified using ICD-10 codes (B03.0-B03.9) and comorbid conditions were also collected. The annual crude incidence rates and age-standardized rates of HZ were calculated using direct standardization to the 2010 Korean-Census population. Negative binomial regression was used to analyze the yearly incidence rate ratio (IRR) and the impact of immune status on disease severity. Healthcare utilization was compared across age groups and comorbid conditions.

Results. The crude and age-sex standardized incidence rate of HZ annually increased over the study period. Such trend was also observed after adjusting for age, sex, immune status, and sociodemographic status (adjusted IRR 1.06, 95% CI 1.01-1.58). The incidence was highest in 65-69 year-olds while the relative increase was high in 11-15-year-olds. The incidence of HZ-associated hospitalizations and complications also steadily increased over time as well as across age groups although the proportions among HZ cases remained stable. Among HZ cases, the risk of complications was higher among elderly population (≥71 years; IRR 1.1-1.23), patients with comorbidities (IRR 1.17, 95% CI 1.14-1.19), and male patients (IRR 1.19, 95% CI 1.09-1.30). The length of hospital stay (median days [range]) was 10 days [6-14] (p = 0.001) was significantly greater in HZ patients with complications than without.

Conclusion. The incidence of HZ has rapidly increased independent of population structure change. It is necessary to establish strategies such as vaccination to reduce the incidence of HZ and efforts should be made to reduce the disease burden among those with comorbidities.

The trend in the incidence of herpes zoster and effect of immune status on Severity and Healthcare Utilization: Population Based Study of South Korea, 2003-2015

Method

We used population-based medical records from the National Health Insurance Service for approximately 55,000,000 subscribers from 2003-2015. An incident case of HZ was defined as the first ever identified case during and severity of HZ was not be well understood. We investigated longitudinal changes in the incidence of HZ and disease severity over time and according to age and comorbidities.

Results.

The crude HZ incidence significantly increased over time from 3.27/1000 person-years in 2000/2002 to 8.69/1000 person-years (IRR per year 1.12, 95% CI 1.01-1.25, Fig. 1). Such trend was also observed after adjusting for age, sex, immune status, and sociodemographic status (adjusted IRR 1.06, 95% CI 1.01-1.58). The incidence was highest in 65-69 year-olds while the relative increase was high in 11-15-year-olds (Fig. 2). There were no significant change in age distribution in the HZ incidence over time.

Incidence of HZ-associated hospitalizations steadily increased over time as well as across age groups (Fig 3). Although the proportions of hospitalization among HZ cases remained stable, incidence of HZ-associated complication also steadily increased over time as well as across age groups (Fig 4). Although the proportion among HZ cases decreases steadily (2007-2015) in 2010; 7.11, IRR 0.97, p = 0.006) suggesting that disease severity was not the main factor for increase in the proportion hospitalization. Among HZ cases, the risk of complications was higher among elderly population (≥71 years; IRR 1.1-1.23), and male patients (IRR 1.19, 95% CI 1.09-1.30). Among the total HZ patient, the number and proportion of immunocompromised host with comorbid disease increased gradually (Fig 5). These immunocompromised host group had higher rates of hospitalization and complicated case than immunocompromised host group (IRR 1.17, 95% CI 1.14-1.19, Table 1). The length of hospital stay (median days [range]) was 10 days [6-14] (p = 0.001) was significantly greater in HZ patients with complications than without.

Conclusion.

The incidence of HZ has rapidly increased independent of population structure change. The elderly and immunocompromised patients have a high disease severity and medical burden. These change in population structure and complication rate of HZ have been observed since 1987. In 2000, one-dose vector vaccine vaccine was included in the NIP for children age 12-15 months old. However, there was no research about the change of the incidence and hospitalization in the development of herpes zoster vaccine. Experience on HZ after HZ vaccine introduction has been collected. The increasing immunocompromised host and extended life expectancy may increase HZ susceptibility. However, the effects of changes in population structure and immune status on the incidence and severity of HZ have no well-studied.

Table 1. Effect of immune status on complication and healthcare utilization among patients with herpes zoster

<table>
<thead>
<tr>
<th>Immune status</th>
<th>N</th>
<th>Hospitalized (N)</th>
<th>Hospitalized %</th>
<th>Complicated (N)</th>
<th>Complicated %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunocompetent</td>
<td>12,000</td>
<td>1,100 (92)</td>
<td>92</td>
<td>300 (26)</td>
<td>26</td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>10,000</td>
<td>900 (90)</td>
<td>90</td>
<td>280 (28)</td>
<td>28</td>
</tr>
</tbody>
</table>

Figure 1. The trend in herpes zoster incidence from 2003 to 2015 in South Korea.

Figure 2. The trend in the age-specific incidence rate per 100,000 person-years among those above 60 years of age from 2003 to 2015, in South Korea.

Figure 3. The trend in herpes zoster hospitalization rate & hospitalization complication rate from 2003 to 2015 in South Korea.

Figure 4. The trend in the age-specific incidence of herpes zoster-associated hospitalization and complication per 100,000 person-years among those above 60 years of age from 2003 to 2015, in South Korea.

Figure 5. The trend in patient number & proportion of herpes zoster with complicated cases.