Surveillance report

SURVEILLANCE OF VARICELLA AND HERPES ZOSTER IN SLOVENIA, 1996 – 2005

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In Slovenia, varicella and herpes zoster infections are case-based mandatorily notifiable diseases. We present surveillance data for a period of 10 years (1996-2005). Incidences of varicella ranged from 456 to 777 per 100,000 population in all age groups. As many as 75% of varicella cases reported were in pre-school children, with children aged three and four years being most affected. The incidence of varicella increased between October and January and was lowest in August and September; the seasonal pattern matches patterns in the school calendar. Herpes zoster was declared a reportable disease in 1995. In 2005, 1,627 cases were notified (81.3/100,000). Female cases outnumbered male. The highest incidence of herpes zoster was noted in elderly individuals over 70 years of age. Complications, such as zoster meningitis and meningoencephalitis, were rarely reported (3.05/1,000,000).

Introduction

Varicella (chickenpox) is a common illness with a relatively distinct clinical picture. Transmission of the varicella virus is by respiratory droplets, aerosol or direct contact with a patient's skin lesions. Varicella is a highly contagious disease with a clinical attack rate of 65% to 85% following household exposure of susceptible individuals [1]. Serological studies across Europe have shown that antibodies to the pathogen are mostly acquired before 15 years of age [2].

Bacterial skin superinfection is the most common complication of varicella, affecting nearly half of all patients [3]. Serious and life-threatening complications, such as varicella pneumonia and encephalitis, rarely occur. Acute cerebellar ataxia is the most common neurological complication of varicella, and occurs in approximately one in 4,000 varicella cases among children younger than 15 years of age. Varicella pneumonia is the most common complication in adults and requires hospitalisation in approximately one of every 400 varicella cases [4].

After infection, varicella zoster virus (VZV) establishes a life-long latency in the cranial and dorsal root ganglia. In approximately 15% of all infected individuals, latent VZV reactivates to cause herpes zoster over a lifetime (HZ) [5]. Triggers for reactivation are poorly understood. Factors that seem to be responsible for increased frequency of HZ include, among others: impaired cell-mediated immunity (CMI), bone marrow and solid organ transplantation, ageing, UV light, injury, stress. Impaired CMI has been generally identified as a factor predisposing to zoster, while the role of other conditions in its development remains to be elucidated.

Varicella and HZ have not been placed on the list of reportable communicable diseases according to the EU Directive. Only six member states have legal provisions for case-based mandatory

notification of varicella, and only two countries provide primary care surveillance data for HZ [6].

Methods

In Slovenia, varicella became a notifiable communicable disease in 1977. Case-based mandatory notification of HZ was enforced by the Communicable Disease Law in 1995. The data collected include demographics (age, sex), date of onset of illness, complications, hospitalisation and outcome. Notifiable varicella complications that are part of the same dataset (ICD-10 codes) include: B01.0 varicella meningitis, B01.1 varicella encephalitis and B01.2 varicella pneumonia. For HZ only two ICD-10 codes are notified, i.e. B02.0 zoster encephalitis and B02.1 zoster meningitis. Deaths are also reported.

Laboratory confirmation of the disease is not required for the notification of varicella and HZ. The descriptive epidemiology of cases notified between 1996 and 2005 is presented.

FIGURE 1

Incidence rate of notified varicella cases by age group, Slovenia, 1996 - 2005

Results

Varicella

The annual number of notified varicella cases ranged from 9,120 to 15,538 (incidence: 456/100,000 to 777/100,000). Females outnumbered males, but the difference was not statistically

TABLE 1

Age-specific hospitalisation rate, Slovenia, 1996-2005

Age group (years)	0	1-4	5-9	10-14	15-19	20-29	+30	All age groups
Hospitalisation rate (per 1000 varicella cases)	19.5	5.0	4.3	3.3	7.8	15.7	23.3	5.8

FIGURE 2

Average monthly number of reported varicella cases, Slovenia, 1996 - 2005

significant (50.4% versus 49.6%). The majority of cases reported (75%) were in pre-school children under seven years of age. The incidence was highest in three year olds [Figure 1].

The rate of serious complications, including pneumonia, meningitis, and meningoencephalitis, was low. The average ten-year incidence of varicella meningitis and meningoencephalitis was 2.1 per 1,000,000 population (all age groups). For varicella pneumonia the incidence was even lower (0.8/1,000,000). The hospitalisation rate, defined as the number of hospitalisations per 1,000 varicella cases, is indicated in Table 1. No death due to VZV has been notified.

The number of notified varicella cases increased each month from October to January, and declined from February to July [Figure 2]. The lowest number of cases was recorded in August and September.

Herpes zoster

HZ was placed on the list of notifiable communicable diseases in 1995. The initial number of reported cases was low but has been steadily increasing. In 2005, 1,627 cases of HZ were notified (81.3/100,000). The highest incidence was recorded in the elderly [Figure 3]. The 10-14 year age group had a notably higher incidence

FIGURE 3

Average age-specific incidence rate of herpes zoster, Slovenia, 1996 - 2005

FIGURE 4

Seasonal distribution of notified herpes zoster cases, Slovenia, 1996-2005

than young adults aged 20-29 years. As expected, more females (59.5%) than males were affected by HZ, and the female incidence was higher in almost all age groups.

The average 10-year incidence of zoster meningitis and zoster encephalitis was 3.05 cases per 1,000,000 inhabitants. Hospitalisation rate, i.e. the number of HZ hospitalisations per 1,000 HZ cases, is shown in Table 2.

HZ infection does not seem to possess a seasonal pattern, yet the largest average number of cases was reported in August and the smallest in February. The difference, however, did not reach statistical significance (Student t-test). There is no clear explanation of why a greater number of cases were notified in the second half

TABLE 2

Age-specific hospitalisation rate, Slovenia, 1996-2005

Age group (years)	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70+	All age groups
Hospitalisation rate (per 1000 herpes zoster cases)	51.3	46.3	22.7	43	38.2	36.3	55	88.8	53.6

of the year than in the first half [Figure 4].

Comments

Varicella and herpes zoster are not obligatory reported diseases in most of the European Union member states. In some states, varicella epidemics or complicated cases only are notified. Some countries collect data on varicella provided by the sentinel surveillance system based on primary care or paediatricians [6]. In Slovenia, the case-based mandatory notification of varicella has been in place for 30 years. Varicella is the most commonly notified communicable disease as almost everyone is infected before reaching adulthood. Case definitions for varicella or HZ have not yet been formulated. Both diseases run a rather typical clinical course. There are only a few illnesses with vesicular rash that may be misdiagnosed as varicella or HZ (e.g. extensive herpes simplex infection).

During the observation period, the overall incidence of notified varicella cases was 456-770/100,000 (650/100,000). The incidence was highest in three-year and four-year-olds (10,400/100,000 and 9,400/100,000, respectively). Children less than one year of age are usually cared for at home, as the mother's maternity leave starts one month before the expected date of delivery and ends 11 months after the birth. According to the 2005 data provided by the Statistical Office of the Republic of Slovenia (<http://www.stat.si/eng/index.asp>), only 14.1% of children under two years of age but 36.7% of three-year-olds attended kindergarten. Increased pre-school attendance coincides with the highest varicella incidence in this age group. In the United States, the overall incidence of varicella recorded through BRFSS (Behavioral Risk Factor Surveillance System) in 1998 was 1,650/100,000 [7]. The age-specific incidence was highest in children aged between one and four years (8260/100,000) and between five and nine years (7640/100,000). BRFSS is an ongoing, random-digit dial telephone survey and gathers information on health characteristics, risks and preventive behaviours. According to the data collected in Canada and the United Kingdom for the period 1979–1997, the average consultation rates for varicella in children aged 0–4 years were 2,345/100,000 population (Canada) and 3,414/100,000 (UK) [8]. The Canadian data were obtained using annual physician billing claims from the province of Manitoba, which has a population of approximately 1,100,000 and a birth cohort of 16,000. The UK data were derived from a sentinel surveillance programme using a representative sample of practitioners throughout England and Wales. The incidence provided by the French sentinel system was 1,000 to 1,350 cases per 100,000 inhabitants, 80% of them belonging to the age group of one to nine years [3]. According to the most recently collected Dutch data (that is, between 2001 and 2002), the average annual incidence of consultations for varicella was 253.5/100,000; it was highest in children aged less than one year (3,101/100,000) and in children aged between one and four years (3,014/100,000). The data were obtained through the sentinel network of general practices covering 1% of the Dutch population.

The overall incidence of notified varicella cases in Slovenia was higher than that obtained through the sentinel surveillance systems in the UK and the Netherlands, but lower than the figures provided by the French sentinel system and BRFSS [2,3,7,8]. The BRFSS collects data through telephone interviews. Theoretically, all subjects with varicella can be identified through BRFSS, that is, both those who consult a doctor and those who do not. Incidences generated by BRFSS are therefore expected to be higher than incidences calculated on the basis of data collected through the sentinel surveillance system on patients who consulted their general practitioner or paediatrician. Limitations of data provided by BRFSS include the potential for recall bias and uncertainty of self-reported diagnosis: the accuracy of the reporting is not validated. The higher incidence of notified cases in Slovenia, compared with data collected through the sentinel system in the UK and the Netherlands, may be attributed to social factors. Consultation rates may vary between countries. Children with varicella are not allowed to attend kindergarten and a parent who may normally work must stay at home with them. In Slovenia, a caregiver must obtain a medical certificate from the paediatrician to claim compensation from the health insurance agency for days missed from work due to child care. It should be pointed out that the number of varicella cases varies from one year to another. Differences in the incidences reported may be due to comparison of different time periods.

Since the 1970s, the average age at infection has decreased notably (data not shown) as a result of a significant increase in nursery and kindergarten attendance [9]. In recent years, the disease has been increasingly notified in adults [9]. A similar trend has been observed in the UK, where the number of varicella cases has doubled in 0–4 year old children and halved in children aged 5–14 years. This downward shift in age at contracting varicella may result from increased social contacts between pre-school children. [10].

Only two cases of meningitis and meningoencephalitis and less than one pneumonia case per million population were notified during a ten-year period. Varicella runs a severe and complicated course in adults and immunocompromised patients. Due to an increasing number of patients treated with immunosuppressive agents and higher number of adult patients with varicella, a higher incidence of notified cases with complications would be expected. The reason of under-reporting severe cases is not clear. The retrospective study analysed hospitalised patients admitted to one tertiary care centre with varicella during a four year period (from 1995 to 1998). Two deaths caused by varicella were identified, giving specific mortality 1 per 30,000 notified varicella cases in Slovenia [11]. Serious complications observed in the case-based mandatory system occurred less frequently than reported in the German study: a crude incidence of severe varicella complications in previously healthy children was 0.8/100,000 [11]. The study showed that the most common complications were neurological complications, with cerebellar ataxia being the most frequently diagnosed condition, followed by encephalitis. The highest age-specific hospitalisation rate for adults with varicella aged over 30 years was reported in the Dutch study [2].

The seasonal distribution of varicella cases is uneven, with the lowest incidence during the 10-week school summer holidays. Summer holidays for primary and secondary schools start on 24 June and end on 1 September. During this period the number of children in kindergarten drops, as most children spend their holidays with parents or grandparents. Therefore, during summer months, children socialise less, and the possibility of viral transmission is reduced. Other school holidays (autumn, Christmas and winter holidays) last only one week, which is too short a period to help reduce the spread of varicella. Two peaks of varicella cases recorded in some countries are attributable to different school calendars [8].

HZ has been on a list of notifiable diseases for 10 years, yet HZ cases have undoubtedly been under-reported. It is difficult to explain why varicella cases are more accurately notified than HZ cases. According to the population-based data, the HZ incidences range from 1.2 to 4.8 per 1,000 population [2,8,12,13]. Older studies reported lower numbers than the more recent ones, most probably as a result of the ageing population in the developed part of the world.

There has been an increase in the HZ incidence along with prolonged longevity in the developed world. In 2005, the notified HZ incidence in Slovenia was 0.81 per 1,000 population, which is six-fold less than the highest incidence published. Most of the cases reported were elderly individuals over 70 years of age. The important thing to note is that teenagers were more frequently affected than young adults, an observation that we are not able to explain. HZ incidence increased with the increasing age in most but not all studies. As reported by Mullooly, the HZ incidence in females

aged 10-17 years was higher than the incidence in the adjacent age group of 18-29 years (217/100,000 vs.177/100,000) [13]. In the UK, the decrease in varicella consultations in school-children coincided with an increase in the HZ incidence in the same age group [8]. Our surveillance data showed higher hospitalisation rates for HZ than for varicella, which accords with the data published by Brisson [8].

Varicella vaccination coverage in Slovenia is very low. The majority of vaccinees are immunocompromised patients and seronegative individuals recently exposed to a child with varicella. Vaccination against varicella is recommended for healthcare workers who are not immune, as in the UK [14]. However, vaccination in line with the current recommendations is practiced in very few healthcare institutions in Slovenia.

An overview of varicella zoster vaccination policies in Europe was provided by the European Sero-Epidemiology Network 2 (ESEN2), which comprises 22 European countries and Australia [6]. Germany is the only European country with routine childhood immunisation against VZV: VZV vaccination by a single dose given at the age of 11-14 months was incorporated into the routine immunisation schedule in July 2004. Three more countries have recently recommended vaccination of children against VZV, and a further five are considering introducing routine VZV immunisation of children.

The policy of universal vaccination against varicella in childhood will undoubtedly help reduce varicella disease in the vaccinees [15]. The introduction of this mass vaccination programme demands meticulous surveillance of varicella and HZ for at least two reasons: a) to document the drop of varicella cases after the introduction of varicella vaccine and to ensure there is no 'epidemiological shift' of varicella cases to older age groups, potentially causing more complications, and b) to monitor the HZ epidemiology. An upward trend in HZ cases may occur without natural boosting of immunity which is currently provided by intensive circulation of VZV in the community. An increase in the number of HZ cases was predicted by a mathematical model and by a population-based study conducted in the United States [16,17]. Frequent contacts with children seem to protect against VZV reactivation [18].

A comparison of our surveillance data and the sentinel data on varicella incidence indicates that a large proportion of actual varicella cases have been reported in Slovenia. The system of reporting HZ cases is much less reliable, and we estimate that, compared with other studies published, only between a quarter and a fifth of all cases are notified. After the introduction of universal vaccination, the case-based surveillance of varicella should continue to identify shifts in age groups, as well as outbreaks and breakthrough infections in vaccinated persons. Before the introduction of a routine varicella vaccination programme, an effort is needed to enhance surveillance of varicella complications and HZ.

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